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THE RECOGNITION OF COARCTATION OF THE AORTA (ADULT TYPE) DURING CHILDHOOD

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THE diagnosis of coarctation of the aorta at any age during life used to be considered quite a feat until King,[1] Blackford[2] and Abbott[3] gave impetus to its clinical recognition. The diagnosis of the condition in childhood, however, is still a rare occurrence. For instance, Blackford,[2] in 1928, wrote that about seventy-eight cases were recognized clinically up to that time, of which four were in children. The youngest of these four was 5 years of age. Between 1928 and the present time there are in the literature[4-25] about forty more authentic cases recognized in adults from the ages of 17 to 66 years. Two of these cases were reported by Walker,[26] dealing with occurrence of coarctation of the aorta in a father aged 49 years, and son, 18 years old. On the other hand, during this same period the number of coarctations recognized in children was only eleven. These children ranged from the ages of 5 to 14 years. It is clear, therefore, that the findings of coarctation of the aorta in children are yet not widely understood.

The usual picture of coarctation presented in the literature concerns adults, and stress is laid on observation for pulsating vessels of the chest wall and x-ray evidence of erosions of the ribs. These striking findings are likely to be absent in the child; they develop only over a period of many years. To depend upon such evidence will mean the oversight of instances of coarctation which might have been discovered early in childhood.

GENERAL REVIEW OF THE LITERATURE

As early as 1907, Carpenter[27] gave a good account of how coarctation of the aorta might be diagnosed. The condition was first described anatomically by Morgagni in 1760. It is a constriction of a varying degree of the aorta at or just distal to the insertion of the ductus

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arteriosus. The ductus arteriosus may be patent or obliterated without influencing the condition. The heart's structure in the so-called adult type of coarctation is normal except for the presence of a bicuspid aortic valve in 25 per cent of the cases, according to Abbott.[3] The adult type is compatible with long life as contrasted to infantile coarctation. Infantile coarctation is the occurrence of extensive and marked narrowing of the aortic arch, with congenital anomalies of the heart making the condition incompatible with life. In 1898 Reynaud considered the constriction to be due to developmental defects of the left fourth and fifth aortic arches. Because of the constriction, collateral circulation occurs which must apparently be already well established when the child is born. Collateral circulation takes place between the left subclavian and innominate arteries and the internal mammary, intercostal and dorsal scapular arteries. The internal mammary connects with the deep epigastric artery and with the aorta. Lewis[28] stressed the interesting facts that despite the resulting hypertension, cardiac hypertrophy is unusual and there is no increased arteriosclerosis demonstrable in the arteries of the upper extremities. He also pointed out how commonly one could feel or see, in adults, the enlarged collateral vessels of the chest wall.

Woltman[29] is credited by Blackford[2] as having first used the absence of femoral pulsations as an aid in diagnosis.

Meckel, according to Fray,[4] is said to have first described the groove-like erosions of the ribs from the enlarging intercostal arteries. This finding can be demonstrated in practically every adult by x-ray evidence. Lombardi reported[30] and I, likewise, report erosion of the ribs in a 5-year-old child, which is the earliest so far in the literature. Fray[4] and others, too, described the x-ray picture of the heart, pointing out the absence of the aortic knob in a postanterior view and the presence of a defect in the aortic arch in the left oblique view. Abbott,[3] in her classic article on coarctation of the aorta, presents a most detailed account of symptoms and physical findings as well as statistics on 200 autopsied patients. Some of the things she pointed out were these: 74 per cent died before they were 40 years old; 60 of the 200 died of congestive heart failure, 38 of rupture of the aorta, 26 of cerebral accidents due to leakage or rupture of an aneurysm of the circle of Willis; and 14 of subacute bacterial endocarditis. The remainder died of miscellaneous causes, two of heart rupture. Lewis[28] warned that individuals with coarctation might come to a physician first because of symptoms of early cardiac failure.

A REVIEW OF CASES REPORTED IN CHILDREN SINCE 1928

I believe I have here every report of coarctation of the aorta recognized in children during life since Blackford's[2] study; and since that time no one has reported more than a single instance of coarctation.

Poynton and Sheldon[31] wrote of an 8-year-old child with the condition, who succumbed from an ulcerative aortitis. The diagnosis was verified by autopsy. Thomson and Lamb[32] reported the occurrence of the condition in a 5-year-old child who died suddenly. Autopsy was not permitted of the head, which probably would have revealed the cause of death, since none was found in the organs of the chest and abdomen. Hampson[33] recognized the condition in a boy 12 years old. Wolffe[34] reported an instance discovered in a 7-year-old child, whose case he followed for ten years. At 17 years the youth was well and without symptoms. As a child this boy also had rheumatic fever. Monterieff[35] reported a boy 6 years of age in whom coarctation was recognized. At the time the report was in print, the child was suspected also of having subacute bacterial endocarditis. Lichtenberg[36] gave details of a 12-year-old girl from our clinic who survived after a very severe cerebral accident followed by hemiplegia. Even now at the age of 19 years she is well and has been working as a nursemaid. She has recovered completely from the hemiplegia.

Vega Diaz et al.[37] reported the occurrence of the condition in a 13-year-old child who apparently was well and without symptoms. Purks[18] reported coarctation in a 14-year-old negro boy who was apparently well and without symptoms. Ferris[19] reported a cerebral death from coarctation diagnosed in a child aged 11 years. The period of observation was just a few weeks. Lian et al.[20] reported a 13-year-old child with apparently no trouble from the condition. Lombardi[30] recognized one case of coarctation in a 5-year-old child.

CASE REPORTS OF COARCTATION OF THE AORTA RECOGNIZED IN CHILDREN, AGED 2½, 3, AND 9 YEARS

CASE 1.—M. H., a girl born April 21, 1935, came to us September, 1937, at the age of 2 years and 5 months because of a severe upper respiratory infection and was admitted to the hospital. She had been seen occasionally in our clinics from the age of 5 months for such conditions as impetigo and mild colds, yet nothing abnormal about the heart was recorded.

Examination revealed a well-nourished girl with no disproportionment in development of lower and upper parts of the body. Her heart was normal in size. A rather loud, somewhat harsh murmur was best heard over the base of the heart at the second left interspace. The murmur was easily heard in the left axillary region and over the left back area. The feet felt distinctly colder than the hands. The femoral pulsations were not palpable. Blood pressure reading in the right arm was 124/86; in the left arm, 128/100. No pressure readings were obtainable in the legs.

An x-ray film failed to reveal erosions of the ribs. The electrocardiogram revealed a marked left axis deviation with a diphasic QRS in Lead II.

CASE 2.—G. H., a boy born June 13, 1934, came to us June, 1937, at the age of 3 years. He was diagnosed as having a congenital heart abnormality from the age of 8 months. There was no history of cyanosis, and the boy had no physical complaints. He was normally active.

Examination revealed a well-nourished and well-developed boy. His heart was not enlarged. A murmur was best heard at the apex, rather loud, but not widely transmitted. It was easily heard over the back, especially near the left scapular region. Pulsations in the groin and blood pressure readings in the legs were not obtainable. The blood pressure reading in the right arm was 140/70; in the left arm, 145/105.

An x-ray picture taken in June, 1937, showed a heart of about normal size, somewhat flask-shaped. There was no erosion of the ribs. The electrocardiogram showed a diphasic QRS complex in Leads I and III. There was no evident heart preponderance.

CASE 3.—R. M., born July 18, 1928, came to us first in March, 1933, at the age of 4½ years for a general examination. At this time, he apparently had no symptoms. About April, 1937, at the age of 9, he began to complain of marked pain in his legs after walking short distances and occasionally of pain beneath the ribs on his left side. Although he was seen every three months in the cardiac clinic, coarctation of the aorta was overlooked for about five years.

Examination revealed a robust looking boy of high color. The heart was not enlarged. There was an apical heart murmur described as soft but suggestive of rheumatic origin. Extrasystoles were present from time to time. Femoral pulsations were absent. The blood pressure reading in the right arm was 140/80; in the left arm, 154/100. No readings were obtainable in the legs.

An x-ray film taken when the patient was 5 years old showed early erosions of the lower margins of several ribs, but no one recognized the nature of the findings in the plate until he was properly diagnosed. At the age of 9 years these erosions were far more evident. The heart was normal in size in both plates.

The electrocardiogram showed left heart preponderance and ventricular extrasystoles.

COMMENT

I do not believe it can be overemphasized that the diagnosis of coarctation of the aorta was made correctly in the aforementioned children because the possibility was kept in mind. Before these cases were found, only one had been discovered in our clinics in the past ten years. The far more common reports of the condition in adults would indicate that it was being overlooked in childhood.

One should become aware of the fact that in children, with few exceptions, no symptoms are created by the adult type of coarctation. But when symptoms are present, they may be distinctive, as in Case 3. Intermittent claudication should suggest the possibility of coarctation.

The general physical examination will practically never disclose anything unusual. Each of these three children looks normal externally. In retrospect it is easy to attach significance to the heightened color of R. M.'s (Case 3) face and the definite colder feel of M. H.'s (Case 1) legs as compared to her arms. The pulsating, tortuous vessels seen on the chest walls of adults with coarctation take years to develop.

Heart enlargement will not be present because of coarctation. There must be some other cause to account for any dilatation or hypertrophy which is present. And I do not believe that the heart murmur one hears in a child with coarctation may be described as typical. Perhaps the

most characteristic thing is that the murmur is heard in the back over the left scapular region, although this was not true in Case 3. By different examiners, the murmur in Case 1 was labeled functional and congenital. By every examiner the murmur in Case 3 was labeled as possibly rheumatic in origin. In all three cases the notes about the murmurs indicated that the examiners were a little puzzled as to the exact nature of the heart sounds.

The simplest and most direct method of making the diagnosis in a suspected instance of coarctation is to feel for femoral pulsations. I palpated for the femoral arteries in every new case referred to the heart clinic. Normally, the pulsations of the femoral artery in a child are very easily found. In the presence of a constriction of the aorta these pulsations are absent or, at least, are very difficult to obtain. To my surprise, I discovered Cases 1 and 2 within a few months of each other by noting the absence of femoral pulsations. In a like manner, Dr. Mandel L. Spivek diagnosed the condition of R. M. (Case 3).

Blood pressure readings when elevated will also give one a clue. Furthermore, in coarctation of the aorta the blood pressure readings of the arms are always higher than those of the legs. Normally, the reverse exists. Most frequently, no readings at all are obtainable in the legs as is true in the three cases I have reported.

X-ray pictures probably will not show erosions of the ribs from the intercostal arteries if the diagnosis is made as early in life as 3 years of age. In these three children, only the oldest had demonstrable erosion of the ribs. Fortunately, an x-ray film of the heart was taken of Case 3 when the patient was 5 years old, and in that picture the telltale erosions were definite, although very slight.

The electrocardiogram is no aid in diagnosis.

I have come to consider palpation for femoral pulsations just as much a part of a routine cardiac examination as palpation of the apex beat or percussion of the heart borders. The employment of this simple procedure in heart examinations will, I am sure, increase the number of instances of coarctation of the aorta recognized in childhood.

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THE RELATION BETWEEN PLASMA ASCORBIC ACID CONCENTRATION AND DIET IN THE NEWBORN INFANT

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VITAMIN C is not usually added to the diet of the artificially-fed infant until the second or third month of life. According to Holt and McIntosh,[1] "infants who are fed on sterilized or pasteurized milk should always be given orange juice or some other antiscorbutic food from the second month onward." A League of Nations commission[2] has recently recommended that vitamin C should be "given as from the age of three months," with no differentiation between breast and artificial feeding. The purpose of this paper is to present evidence of the close relation, in newborn infants, between the dietary supply and plasma concentration of ascorbic acid.

That woman's milk contains a significant amount of ascorbic acid is evident not only from clinical observations, but also from experimental investigation by Selleg and King[3] and others; scurvy is rare in the breast-fed infant. Similar observations indicate that the pasteurized, boiled, or evaporated cow's milk usually used for the preparation of infant feeding mixtures has a low ascorbic acid content.[4, 5, 6] There has been in the past no direct measurable chemical evidence that the vitamin requirement differs in breast-fed and artificially fed infants. Consequently, it seemed probable that the ascorbic acid reserve of the infant would begin to be depleted from the inception of a dietary regime which is lacking in vitamin C substance, and that this depletion might be reflected by a diminution of its concentration in the blood plasma.

The plan of study herein reported was as follows: Fifty normal, full-term infants were selected for study at the end of the first two weeks of life. Group I was composed of twenty-one infants who were satisfactorily nursed at the breast. Group II contained nineteen infants who were entirely artificially-fed for the last four or more days because of an abrupt cessation of breast feeding. The artificial feeding was a twice-pasteurized cow's milk-karo-water mixture.* Group III consisted of ten infants similar to those in Group II, but who received daily supplements of ascorbic acid for the duration of artificial feeding.† Three infants were given 20 mg. of ascorbic acid daily, three, 30 mg. daily, and four, 75 mg. daily. Ten or 25 mg. of ascorbic acid were added to the feeding

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*The composition was: milk (2 per cent or 4 per cent) 12 oz., water 5 oz., karo 1 oz.

†The ascorbic acid was supplied by Merck & Co., Inc., Rahway, N. J.

mixture two or three times daily, about fifteen minutes before it was given to the infant. During this time complete solution occurs, but the oxidative loss of ascorbic acid is less than 5 per cent.

METHOD

The plasma ascorbic acid concentration was determined by the micromethod of Mindlin and Butler.[7]* This procedure measures colorimetrically, by means of a photoelectric microcolorimeter, the amount of reduction of 2, 6-dichlorophenol indophenol caused by the ascorbic acid in 0.1 c.c. of plasma. Blood samples were collected at varying intervals with respect to the previous feeding. This procedure is justified because it has been found[9] that the small amount of ascorbic acid ingested by a two-week-old infant in a single feeding of breast milk (5 mg. or less) does not result in a rise in the plasma concentration. However, in no instance was a sample taken from an infant who received 10 or 25 mg. of ascorbic acid in a feeding mixture within sixteen hours of the last dose.

RESULTS

The experimental results are presented in Tables I, II and III. The average plasma ascorbic acid concentration in Group I (normal, breast-

TABLE I

PLASMA ASCORBIC ACID CONCENTRATION IN BREAST-FED INFANTS

GROUP I

CASE NO.	AGE (DAYS)	PLASMA ASCORBIC ACID (MG. %)	REMARKS
1	14	1.6	
2	13	1.3	
3	14	1.2	Cesarean section
4	13	1.2	Cesarean section
5	14	1.1	
6	13	1.1	
7	13	1.1	
8	13	1.1	
9	13	1.1	
10	13	1.1	
11	13	1.0	
12	14	0.9	
13	13	0.9	
14	13	0.9	
15	14	0.8	
16	13	0.8	Complementary feedings, 5th to 7th days
17	13	0.7	
18	13	0.7	Complementary feedings, 6th to 8th days
19	13	0.7	
20	13	0.6	
21	13	0.6	
		Average: 1.0	

*Recent work[8] has shown that the use of potassium cyanide in this determination is unnecessary and may under certain conditions introduce error. Under the conditions prescribed by the method, the error in plasma values due to the additions of potassium cyanide may vary from 0.0 to 0.1 mg. per cent and is therefore insignificant.

TABLE II

PLASMA ASCORBIC ACID CONCENTRATION IN ARTIFICIALLY-FED INFANTS

GROUP II

CASE NO.	AGE (DAYS)	ARTIFICIAL FEEDING (DAYS)	PLASMA ASCORBIC ACID (MG. %)	REMARKS
1	12	5	0.7	
2	12	5	0.6	
3	13	6	0.5	
4	13	5	0.5	
5	13	4	0.4	Complementary feedings for 4 days before breast feedings discontinued.
6	13	7	0.4	
7	13	7	0.4	
8	15	8	0.4	
9	14	9	0.4	
10	15	5	0.3	
11	13	8	0.3	
12	20	7	0.3	
13	13	5	0.2	Complementary feedings for 6 days.
14	13	6	0.2	Complementary feedings for 2 days.
15	13	8	0.2	
16	8	8	0.2	
17	14	9	0.2	
18	13	13	0.2	
19	19	19	0.1	
		Average:	0.3	

TABLE III

PLASMA ASCORBIC ACID CONCENTRATION IN ARTIFICIALLY-FED INFANTS RECEIVING DAILY ASCORBIC ACID SUPPLEMENT

GROUP III

CASE NO.	AGE (DAYS)	ARTIFICIAL FEEDING (DAYS)	ASCORBIC ACID SUPPLEMENT (MG. PER DAY)	PLASMA ASCORBIC ACID (MG. %)
1	14	8	20	0.4
2	13	7	20	0.5
3	13	6	20	0.6
4	13	8	30	0.6
5	13	7	30	0.7
6	13	7	30	0.8
7	13	7	75	0.7
8	13	8	75	0.6
9	13	8	75	0.8
10	13	9	75	0.7

fed infants at the age of about 2 weeks) was 1.0 mg. per cent, with a range from 0.6 to 1.6 mg. per cent. Similar determinations on infants who had received pasteurized artificial feedings for varying periods of time (Group II) revealed considerably lower values; i.e., in fourteen infants who had received no breast milk for five to nine days, the average plasma ascorbic acid concentration was 0.4 mg. per cent. Those who were artificially fed for longer periods had still lower concentrations. One infant, 19 days of age, artificially fed from birth, had 0.1 mg. per

cent of ascorbic acid in the plasma. The infants who were artificially fed and received daily supplements of ascorbic acid (Group III) had somewhat higher plasma ascorbic acid concentrations than those in the unsupplemented group (II) who had received artificial feedings for the same period of time.

DISCUSSION

The significance of low plasma ascorbic acid concentrations is not clear. From the work of Ingalls[10] it is evident that in infantile scurvy the amount of ascorbic acid in the plasma is so small that it approaches the limit of accuracy of the determination. However, there is a wide range in normal individuals. With increasing experience with the *method*, it has been found that for normal individuals the ascorbic acid content of the plasma gives a reliable index of the dietary intake of the vitamin. On this basis a standard has been established for normal children and adults: with optimal vitamin C intake the plasma ascorbic acid concentration is 0.6 mg. per cent or higher; with suboptimal and deficient intakes the concentration falls below this level to an extent dependent upon the degree and duration of the deficiency; with clinical scurvy it approaches zero.

Although the correlation between the depletion of the bodily store of ascorbic acid, as measured by its concentration in the plasma, and pathologic physiology and histologic change has not been established, nevertheless, it is probable that the optimum state for the individual is one of abundance rather than one of paucity. The numerous tests for "saturation,"[11] based upon the measurement of the urinary excretion of ascorbic acid, and the absence of a syndrome of hypervitaminosis C indicate that the substance is readily excreted and is nontoxic.

The data presented show that breast-fed infants, at least for the first two weeks of life, have an ascorbic acid intake sufficient to maintain a plasma concentration which is considered optimal for older children and adults. The artificially-fed infants of the same age group do not maintain this concentration when the dietary supply of ascorbic acid is deficient. These infants do not have scurvy. Infantile scurvy is a clinicopathologic entity with characteristic signs and symptoms, all of which were absent from this group. But these infants are receiving scorbutogenic diets and are in, or are approaching, a state of asymptomatic ascorbic acid deficiency which is the forerunner of clinical scurvy. The addition of sufficient ascorbic acid to the diet of the artificially-fed infant abolishes this state and restores the optimal concentration of ascorbic acid in the plasma.

The plasma concentrations in the artificially-fed infants who received ascorbic acid are near to the lower limit of the optimal range. These low values may be related to the sixteen-hour interval between the last administration of ascorbic acid and the taking of the blood sample. The

breast-fed infants received a small amount of ascorbic acid with every feeding, that is, at intervals of four hours. Hence they were never subject to a sixteen-hour depletion period, which in the very young infant may cause a slight fall in the plasma level.

For optimal nutrition it seems indicated that newborn infants who are fed pasteurized artificial feedings should receive a daily supplement of ascorbic acid from the beginning rather than after two or three months.

SUMMARY

1. The plasma ascorbic acid concentration of normal two-week-old infants on breast feeding averages 1.0 mg. per cent.

2. The plasma ascorbic acid concentration of normal two-week-old infants on artificial feeding for about one week averages 0.4 mg. per cent. Lower values result from longer periods of artificial feeding.

3. The addition of sufficient ascorbic acid to the diet prevents the fall in plasma concentration invariably found with pasteurized feeding.

I wish to thank Dr. A. M. Butler and Dr. A. T. Shohl for their valuable criticisms and suggestions during the course of this work.

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VITAMIN C CONTENT OF THE BLOOD IN NEWBORN INFANTS

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LABORATORY methods for the estimation of the vitamin C content of the blood now make it possible to study the amount of this vitamin under various conditions. Studies that have been made on the vitamin C content of the blood of the newborn infant show dissimilar values. The majority of these have been made on cord blood. Abt, Farmer, and Epstein[1] showed almost identical values of cord blood vitamin C and blood obtained from the mother. Nielsen[2] has found more in the fetal blood than in the maternal blood. These represent the two extremes, and other determinations will be discussed later. It seemed to us that the blood values for the newborn infant should be determined throughout the newborn period, and, if possible, these values should be correlated with those of the mother.

PROCEDURE

Almost all methods of determination of vitamin C depend upon its reducing power, even in an acid medium. Some methods also estimate the entire vitamin rather than the reduced vitamin. Values obtained for either of these quantities will be different and will account for different results obtained.

After various trials of different methods of blood vitamin C determinations, it was decided to use the method of Abt and Farmer. We do not wish to enter into any discussion of the various methods of determination for this vitamin. It was sufficient for us that this method gives constant values for all individuals who should have a constant vitamin C blood value, that is to say, individuals who have had adequate vitamin C intakes. Individuals who have had inadequate vitamin C intakes consistently show lower values, and in the one case of proved infantile scurvy that we had an opportunity to study the blood vitamin C value was lowest of all.

Both the micro- and macromethods were used. In the mothers and other adult cases both methods were used on each patient. In the infants both interval determinations were made by the micromethod, with the macromethod used as a check on one interval or the other. It was found that the average difference between the two methods was approximately 0.1 mg. per cent. Blood was drawn from the newborn infants on the second and eighth days of life, and on the same days from their mothers. These estimations were made immediately after withdrawal of the blood.

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TABLE I

BLOOD VITAMIN C VALUES

	VITAMIN C IN MG.								VITAMIN C AVERAGE OF TOTAL
	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.1	
123 infants	3%	14%	12.5%	18%	27%	13%	8%	4%	0.753 mg.
105 mothers	0	7%	12%	15%	27%	14%	9%	10%	0.884 mg.
51 adults	6%	10%	6%	19%	12%	8%	10%	29%	0.990 mg.

RESULTS

Table I shows the results obtained on the vitamin C blood values of fifty-one dispensary patients, from 6 to 60 years of age, presumably on an adequate diet. The members of this group, however, who were under 0.6 mg. per cent showed an interesting dietary history. The three mem-

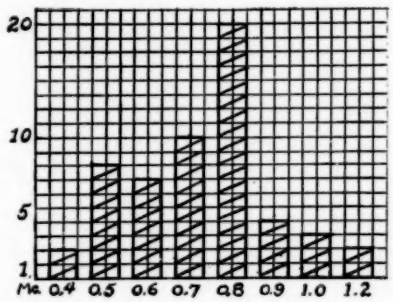

Fig. 1.—Vitamin C values of the blood in newborn infants.

Fig. 2.—Vitamin C values of the blood in post-partum mothers.

bers whose blood values were under 0.5 mg. per cent were negro males from 44 to 50 years of age. Dietary history revealed they never ate oranges and rarely had fruit of any kind. The six members of the group between 0.5 mg. and 0.6 mg. per cent were white males, between 38 and 58 years of age. Their dietary history was that they ate fruits and oranges only occasionally. As a matter of interest, all of these individuals came to the clinic because of irritability, nervousness, and poor appetite of years' duration. They were all markedly thin, and the negroes were undernourished. However, these patients did not come to the dispensary for dietary management. They had no definite symp-

toms of scurvy, and we felt that in all fairness to the study they should be included in the average of the general control group. The average blood vitamin C value for this group was 0.99 mg.

Table I also shows vitamin C blood values of 123 infants and 105 mothers. These mothers are of moderate economic circumstances and pay a set fee for their entire hospital service. Their vitamin C intake is discussed in Table VIII. It may be considered on the whole as adequate. The average blood vitamin C values of these mothers was 0.884 mg. and of the infants, 0.753 mg. Figs. 1 and 2 show that the infant tends toward the same value as his mother.

Table II shows the direct comparison of the blood vitamin C values for

TABLE II

BLOOD VITAMIN C VALUES OF MOTHERS AND INFANTS

Mothers' vitamin C 72 mothers	0.5 mg. to	0.6 mg.	0.7 mg.	0.8 mg.	0.9 mg.	1.0 mg.	1.1 mg.
Percentage of infants in group 72 infants		21%	14%	28%	15%	11%	11%
Average vitamin C of infants		0.59	0.68	0.77	0.85	0.89	1.06

TABLE III

INFLUENCE OF BLOOD VITAMIN C ON BREAST MILK PRODUCTION

Mother—vitamin C value	0.5 mg.	0.6 mg.	0.7 mg.	0.8 mg.	0.9 mg.	1.0 mg.	1.1 mg.
Percentage of mothers	5.5%	15%	14%	28%	15%	11%	11%
Breast milk—ounces	30	48.8	40.1	45.8	37.8	36.3	45

TABLE IV

INFLUENCE OF BLOOD VITAMIN C OF MOTHER ON BIRTH WEIGHT OF INFANT

	BIRTH WEIGHT OF BABY IN LB.				
	5 to 6	6 to 7	7 to 8	8 to 9	9 to 10
Percentage of infants	1.5%	8%	49%	33%	7%
Average vitamin C of infant	0.95	0.81	0.74	0.85	0.80

72 individual mothers and their infants. This shows that each individual baby has practically the same vitamin C blood value as its mother. Table III compares the amount of breast milk produced by each mother and her blood vitamin C value. There is no correlation between the amount of blood vitamin C and the amount of breast milk produced. Table IV compares birth weight and the blood vitamin C of the infants. There is no correlation for the normal infant, but Table V, giving the values for seven premature infants, shows that for the majority of these infants the blood vitamin C value is lower than the expected average for normal infants.

TABLE V

BLOOD VITAMIN C VALUES IN PREMATURE INFANTS

AGE	WEIGHT	BIRTH WEIGHT	VITAMIN C (MG.)
1 day	4 lb. 10 oz.	4 lb. 10 oz.	0.40
5 days	5 lb.	5 lb. 2 oz.	0.53
5 days	4 lb. 12 oz.	5 lb. 2 oz.	0.88
8 days	4 lb. 9 oz.	4 lb. 13 oz.	0.63
13 days	3 lb. 15 oz.	3 lb. 15 oz.	0.55
26 days	5 lb. 8 oz.	5 lb. 6 oz.	0.75
27 days	6 lb. 2 oz.	4 lb. 15 oz.	0.58

Table VI compares the amount of breast milk received and the blood vitamin C values for the infants on the second day, with their range during the week. These infants received nothing but mother's milk and water. This shows that there is a slight gain with increasing breast milk, and a slight loss if the breast milk is insufficient.

TABLE VI

EFFECT OF BREAST MILK RECEIVED ON BLOOD VITAMIN C VALUES OF 72 INFANTS (ESTIMATIONS MADE ON THE SECOND AND EIGHTH DAYS)

Mother's milk in ounces (6 days)	0 to 30	30 to 40	40 to 50	50 to 60	60 to 70
Number of infants	13	17	19	16	6
Number of infants gaining vitamin C	2	7	12	10	5
Amount vitamin C gain in mg.	0.035	0.075	0.099	0.157	0.175
Number of infants losing vitamin C	11	10	7	6	1
Amount of vitamin C loss in mg.	0.177	0.129	0.067	0.066	0.017

Table VII shows the vitamin C blood values in infants who were diagnosed as suffering from cerebral hemorrhage and in their mothers.

TABLE VII

BLOOD VITAMIN C VALUES IN MOTHERS AND IN INFANTS WITH CEREBRAL HEMORRHAGE

NO.	MOTHERS VIT. C	INFANTS VIT. C	RESULT
1	0.63 (diabetic)	0.46	Recovered
2	0.66	0.62	Died—Autopsy showed cerebral hemorrhage
3	0.77	0.50	Recovered
4	0.70	0.57	Recovered
5	0.80	0.60	Recovered
6	0.70	0.47	Recovered
7	0.82	0.55	Recovered
8	0.76	0.60	Recovered

Table VIII shows the effect of citrus fruit or adequate vitamin C intake during pregnancy on the blood vitamin C value of the mother after delivery. In the group designated as "excellent," the intake was equivalent to one orange a day; "good," three oranges a week; "fair," one orange a week, and "poor," barely any citrus fruits at all. This table needs no further explanation, and the results are quite striking.

TABLE VIII

EFFECT OF DIET ON THE BLOOD VITAMIN C OF POST-PARTUM MOTHERS

	EXCELLENT	GOOD	FAIR	POOR
	1.62	0.75	0.65	0.46
	1.85	1.75	0.76	0.50
	2.40	0.68	0.56	0.63
	2.10	1.21	0.74	0.58
	2.50	0.75	0.72	0.65
Citrus fruit intake	1.16	0.80	0.81	0.61
	1.50	0.76	0.75	0.55
	1.87	1.25	0.78	0.45
	1.93	0.76	0.67	0.49
		0.88	0.83	
		0.99		
		1.05		
Average vitamin C value	1.88	0.969	0.727	0.546

DISCUSSION

In the control adult group, the limits of blood vitamin C were between 0.4 mg. and 1.8 mg. These individuals were presumed to have adequate vitamin C intakes, but the dietary history of the members of this group below 0.6 mg. per cent has been discussed. Since 76 per cent of this group have blood vitamin C values between 0.5 mg. and 1.2 mg., we may assume that these figures are the average blood vitamin C values for the normal individual. In individuals with inadequate vitamin C intakes the blood value always fell below 0.65 mg., and in the one infant with proved infantile scurvy the blood vitamin C value was 0.4 mg. The limits of blood vitamin C values for the maternal group were between 0.5 mg. and 1.4 mg. Since 72 per cent of these values are between 0.8 mg. and 1.2 mg., these figures may be assumed to be the average for post-partum mothers. In the newborn infant the blood vitamin C values were between 0.4 mg. and 1.2 mg. Since 78 per cent of these values are beween 0.5 mg. and 0.9 mg., this may be assumed to be the average for this group. The general average for the mothers is slightly below that of the adults, and the average for the infants is similar to the mothers. The figures show graphically that the general tendency of the blood vitamin C value of the infant is similar to that of the mother.

While the above results will show a general tendency in comparison with blood vitamin C values, they are not of as much value as the comparison of the values for each individual mother and child. This is shown in Table II, where it will be observed that in almost every case the newborn infant, with few individual variations, has a blood vitamin C value similar to that of his mother. Besides the authors mentioned before, Wahren and Rundquist[3] obtained higher blood vitamin C values for the newborn infant than for the mother. The average blood vitamin C value in seventeen mothers was 0.158 mg. and in the infant, 0.347 mg. A different method of determination of blood vitamin C was used (photo-

metric methylene blue). Nielsen, using a similar method, found the blood vitamin C in forty-one mothers to be lower than in nonpregnant women, and in fetal blood a value eight times higher. By the same method, Braestrup[4] found the cord blood values to be 0.9 mg. in seventy-five infants, while the mothers blood vitamin C values averaged 0.36 mg.

There are two possible explanations for these differences between their results and ours: First, the estimations on the mothers' bloods were made during labor, and there is considerable evidence that labor, among other factors, temporarily reduces the amount of blood vitamin C. Second, the difference in method. Fujita and Ebihara,[5] who have made a comparison of the different methods for determining blood vitamin C content, state that with methylene blue titration a smaller quantity of blood may be used but that it always gives lower values than other methods, such as titration with 2:6-dichlorphenol indophenol. This might well explain the results obtained by Abt in the five mothers and their infants, whom he studied. These values were obtained on cord blood. The values he obtained for individual mothers and infants are quite similar to ours.

We are unable to find that the amount of blood vitamin C in the mother had any effect on the amount of milk that she produced. There is no particular reason that it should do so. An adequate vitamin C intake by the mother might affect the quality of her milk but not the quantity.

In the normal baby there was no correlation between the size of the baby and his blood vitamin C value, that is, a larger baby does not have a higher blood vitamin C value than a smaller one. In the findings of the few small babies studied, we were interested to discover comparatively high blood vitamin C values. For this reason the blood vitamin C values were determined on seven premature infants on different days of life. Instead of being higher, they were considerably lower than the average. Giraud[6] found that the younger the fetus, the higher the vitamin C content of its tissues. Rohmer[7] found the content of the cerebrospinal fluid to be about twice as high in six premature infants as six full-term infants. Certainly in the human fetus, as judged by the blood vitamin C in the premature infant, there is no tendency to store up vitamin C in fetal life.

There is a slight but definite increase in blood vitamin C value of the newborn infant throughout the first week of life, with sufficient mother's milk. Obviously this milk should be from a mother who has an adequate vitamin C intake. If a newborn infant has an adequate blood vitamin C value and obtains adequate milk from a mother on an adequate vitamin C intake, the infant should be amply protected from vitamin C deficiency. This has been found also by Widenbauer and Kuhner.[8]

We present our findings of the low blood vitamin C values in cerebral hemorrhage of the newborn infant but do not wish to draw any conclusions on such a small number of cases. We do feel, however, that the fact that eight newborn babies with a diagnosis of cerebral hemorrhage, whose mothers' blood vitamin C values are, like their infants, below the average, is worthy of note. It may be argued that the diagnosis of cerebral hemorrhage is questionable. We can only prove one case, which came to autopsy, but by the usual methods of making such a diagnosis we believe these infants suffered from such a condition. One mother had a very inadequate intake of vitamin C. She suffered from diabetes. After low blood vitamin C values had been found consistently in several cases, we made it a practice to give all infants with a diagnosis of cerebral hemorrhage cevitamic acid after the blood vitamin C was taken. The fact that these infants recovered proves nothing, as the other infants before this recovered without this treatment. We do feel that the factor of a vitamin C adequate intake in the mother may have some bearing on the condition of the child at birth. Could not a low blood vitamin C be a factor in the fragility of the cerebral capillaries if any extra strain was put on the system?

Finally, we arrive at the question of what all these findings mean. Certainly all of these infants were clinically normal. We never see clinical signs of scurvy before six months of life, and even then an infant on an inadequate vitamin C intake may not develop scurvy. However, there have always been factors in infantile scurvy that were never completely understood. May it not have been that those infants who began with a higher blood vitamin C value were better protected at a later time? How can we give a newborn infant an adequate vitamin C blood value? It clearly depends on the blood vitamin C of the mother, and this can be controlled by her vitamin C intake. As shown in Table VIII, the blood vitamin C of the mother can be tripled by an adequate citrus fruit intake, and this blood vitamin C value may be imparted to her child.

CONCLUSIONS

In 123 infants the average of two determinations made on the second and eighth days of life was 0.753 mg. In 105 mothers of these infants the average was 0.884 mg., and in fifty-one miscellaneous adults the average was 0.99 mg. In a comparison of seventy-two mothers and their infants, it was found that the amount of vitamin C in the infant's blood is directly determined by the mother's blood vitamin C value, and the infant's blood will be, on the average, similar to the mother's. The amount of vitamin C in the mother's blood has no influence on her production of breast milk, on the gain or loss of the infant, or any influence on the infant's birth weight. The birth weight of the infant does not influence the amount of its blood vitamin C, but, providing the mother has an

average amount of blood vitamin C, a gain in weight by the infant taking her breast milk is followed by a small gain in the infant's vitamin C blood content.

Mothers having a liberal vitamin C intake during pregnancy will show a high vitamin C blood content after delivery, and this decreases in proportion as the mother's diet is deficient in vitamin C.

These findings indicate that the amount of vitamin C existing in the mother's blood depends on her diet during pregnancy, and this amount determines the quantity of vitamin C in the blood of her infant. The normal infant tends to the same vitamin C content of the blood as its mother. Seven infants suffering with a cerebral hemorrhage had blood vitamin C values of below 0.62 mg. In certain mothers with a low or threshold value of blood vitamin C, the infant may show a blood vitamin C value that is lower than is consistent with accepted normal values.

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952 NORTH MICHIGAN AVENUE

THE INCIDENCE OF HEMOLYTIC STREPTOCOCCI IN THE TONSILS OF CHILDREN AS RELATED TO THE VITAMIN C CONTENT OF TONSILS AND BLOOD

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SINCE methods have been devised for the accurate determination of vitamin C (ascorbic acid) in the urine and in the blood, numerous reports have been published dealing with the vitamin C content of urine and blood in a number of diseases.

In 1934 Rinehart and Mettier[1] cited experimental, epidemiologic and clinical data in favor of a theory that vitamin C deficiency may be a necessary accompaniment of rheumatic fever. In 1936 Abbasy, Hill, and Harris[2] reported on vitamin C studies in 107 children with active rheumatic fever. Their interpretation of the results is that with the infection which underlies rheumatic fever there is a greatly increased metabolic use of vitamin C and a correspondingly lowered degree of "saturation" of the body tissues. Other studies, notably those of Sendroy and Schultz,[3] do not agree with these observations. It does appear, however, that vitamin C deficiency may play some part in the course of certain infections as well as being the causative factor in scurvy.

In view of the fact that hemolytic streptococci have been associated with the causative factors in rheumatic infections, and that vitamin C metabolism may be influenced by infections, it seemed worth while to study the relationship of the incidence of hemolytic streptococci of the tonsils with the amount of vitamin C found in the blood and in the tonsils of these subjects. If subclinical scurvy can be recognized by a lowered content of vitamin C in the blood, as has been suggested by Abt,[4] it was proposed that there might be some measurable increase of infection in the individuals who show deficient amounts of vitamin C in the blood. The present study was undertaken to determine if any relationship in children exists between the level of vitamin C stored in the blood and the presence of hemolytic streptococcus infection in the tonsils.

A group of 123 children was utilized for this purpose. They ranged in ages from 6 to 16 years. They had been selected by school physicians for various reasons to have their tonsils and adenoids removed. All were admitted to the hospital the afternoon before operations were to be performed. Soon after admission to the hospital 5 c.c. of blood were withdrawn from the vein of each patient. This was examined the following morning for a quantitative determination of vitamin C. This

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procedure was adopted after it was ascertained that practically no vitamin C was lost by keeping the blood cooled for fifteen hours. The tonsils were sent to the laboratory immediately after the operation and were prepared for study within three hours after removal. A quantitative determination of the vitamin C of the tonsils was made in a similar way to that of the blood. To determine the presence or absence of streptococci in the tonsils, the surface of the tonsil was seared and then cut with a sterile knife. Loops were taken from this cut surface and streaked on blood agar plates. Subcultures were made to determine the type of streptococci present in the tonsils. Intraperitoneal injections into mice were later made to determine the virulence of these streptococci. The following method utilized by Stephens and Hawley[5] was employed in determining the content of vitamin C of the blood and of the tonsils: To 2 c.c. samples of whole blood were added 2.5 c.c. of 20 per cent acid (18 per cent trichloracetic plus 2 per cent metaphosphoric acid) and 5.5 c.c. of distilled water. The deproteinized filtrate was used for the estimation of ascorbic acid. The ascorbic acid content of the filtrates obtained was determined by rapid titration against a standardized solution of 2:6-dichlorphenolindophenol. The titrations were completed within thirty seconds and were always made in duplicate. Results were expressed as milligrams of reduced ascorbic acid per 100 c.c. of whole blood. In the case of the tonsils, they were rinsed in distilled water, cut into small pieces, and a gram of tissue weighed out. This amount was ground with very fine sand in a mortar, and 5 c.c. of a 20 per cent solution containing 18 per cent trichloracetic acid plus 2 per cent metaphosphoric acid were added. This mixture was shaken for five minutes, then 15 c.c. of distilled water added and the whole mixture shaken again for ten minutes. It was then filtered through No. 1 filter paper, and the clear filtrate titrated against a known quantity of 2:6-dichlorphenolindophenol to determine the amount of vitamin C contained in 100 gm. of tonsillar tissue.

As noted in Table I, the vitamin C content of the blood varies from 0.50 mg. per cent to 1.08 mg. per cent. Similarly the vitamin C content of the tonsils varies from 18.6 mg. to 53.7 mg. per cent. None of the children on whom these determinations were made were acutely ill. More than half of them came from families who were on relief, while the remainder came from homes that were classed in the lower economic strata. It was possible to observe 96 of these 123 children for a period of six months or more after their tonsillectomy to determine something about the amount of vitamin C they obtained in their diet. During this period following the tonsil operation it was also possible to record the incidence of throat and respiratory infections in the children.

A careful study of the figures noted in Table I shows marked variations in the vitamin C values of the blood and of the tonsils. In Charts 1 and 2 this range from low to high is more easily recognized. The presence of hemolytic streptococci in the tonsil was demonstrated in

TABLE I

NO.	PATIENT	AGE	SEX	MONTH	VIT. C OF BLOOD IN MG.	VIT. C OF TONSIL IN MG.	PRESENCE OF HEM. STREP. IN TONSIL	MOUSE VIRULENCE TEST	DIET VIT. C	DICK TEST	HISTORY OF RESPIRATORY INFECTION SINCE TONSILLECTOMY
1	M. R.	9	F	July	0.70	18.6	Positive	Non-vir.	Inadq.	Neg.	Negative
2	J. B.	8	M	July	0.60	19.5	Negative	—	Inadq.	Neg.	Negative
3	R. D.	9	F	July	0.69	30.6	Negative	—	Inadq.	Pos.	Few colds
4	M. C.	11	F	July	0.57	26.6	Positive	Virulent	Adq.	Pos.	One cold
5	E. V.	9	M	July	0.70	30.6	Positive	Non-vir.	Adq.	Neg.	Negative
6	K. G.	7	F	July	0.70	33.6	Positive	Non-vir.	Inadq.	Neg.	Negative
7	H. B.	10	M	July	0.70	40.8	Negative	—	Adq.	Neg.	Negative
8	D. W.	13	M	July	0.91	36.6	Negative	—	Adq.	Neg.	Negative
9	G. B.	13	F	Sept.	0.80	32.6	Negative	—	Inadq.	Pos.	Two colds
10	B. S.	12	F	Sept.	0.60	26.6	Positive	Non-vir.	Adq.	Neg.	Negative
11	R. H.	9	F	Sept.	0.80	30.6	Negative	—	Adq.	Pos.	Negative
12	G. B.	10	F	Oct.	0.75	23.7	Positive	Virulent	Inadq.	Pos.	Negative
13	T. G.	9	M	Oct.	0.63	26.6	Positive	Non-vir.	Adq.	Pos.	Negative
14	T. P.	13	M	Oct.	0.75	26.6	Positive	Non-vir.	Adq.	Pos.	Negative
15	C. A.	13	M	Oct.	0.83	20.0	Negative	—	Inadq.	Neg.	Negative
16	A. S.	11	M	Oct.	0.92	27.0	Negative	—	Adq.	Pos.	Negative
17	F. B.	8	F	Oct.	0.72	39.0	Negative	—	Inadq.	Neg.	Few colds
18	E. S.	11	F	Oct.	0.69	46.5	Negative	—	Adq.	Neg.	Negative
19	A. C.	12	F	Oct.	0.68	29.4	Negative	—	Inadq.	—	Two colds
20	J. C.	12	F	Oct.	0.65	40.0	Negative	—	Inadq.	Pos.	Negative
21	C. A.	10	M	Oct.	0.71	32.6	Negative	—	Inadq.	Neg.	Negative
22	G. S.	8	F	Oct.	0.64	27.1	Negative	—	Adq.	Pos.	Negative
23	N. S.	11	M	Oct.	0.82	36.6	Positive	Non-vir.	Adq.	—	Negative
24	K. M.	9	F	Oct.	0.73	35.1	Negative	—	Adq.	Pos.	Negative
25	D. P.	13	F	Oct.	0.82	26.5	Positive	Virulent	Adq.	Pos.	One cold
26	L. S.	13	M	Oct.	0.67	39.9	Negative	—	Adq.	Pos.	Many colds
27	R. D.	11	M	Oct.	0.78	30.6	Positive	Non-vir.	Adq.	Pos.	One cold
28	M. P.	8	F	Oct.	0.66	45.0	Positive	Non-vir.	Adq.	Neg.	Many colds
29	M. G.	10	F	Oct.	0.64	43.6	Positive	Virulent	Adq.	Neg.	Sore throats
30	B. M.	11	F	Oct.	0.69	35.1	Positive	Virulent	Inadq.	Neg.	Sore throats, colds
31	L. D.	13	F	Oct.	0.67	44.1	Positive	Non-vir.	Inadq.	Neg.	Many colds

TABLE I—CONT'D

32	C. A.	10	M	Oct.	0.80	36.6	Negative	—	Inadq.	Neg.	Negative
33	J. L.	12	M	Oct.	0.93	26.5	Negative	—	Adq.	Neg.	Few colds
34	L. M.	8	M	Oct.	0.76	28.0	Positive	Non-vir.	Inadq.	Pos.	Negative
35	J. H.	9	M	Oct.	0.83	30.6	Positive	Non-vir.	Inadq.	Neg.	Discharging ears
36	L. D.	9	F	Nov.	0.80	35.1	Positive	Non-vir.	Adq.	Neg.	Many colds
37	J. T.	13	M	Nov.	0.82	23.7	Positive	Non-vir.	Inadq.	Pos.	Negative
38	M. L.	13	F	Nov.	0.89	32.7	Negative	—	Adq.	Neg.	Negative
39	C. H.	10	M	Nov.	0.80	23.7	Negative		Adq.	Neg.	Many colds
40	G. S.	11	F	Nov.	0.71	39.9	Positive	Non-vir.	Adq.	Neg.	Negative
41	J. G.	13	M	Nov.	0.69	33.6	Positive	Non-vir.	Adq.	Neg.	Negative
42	R. M.	15	M	Nov.	0.62	35.1	Positive	Non-vir.	Adq.	Neg.	Negative
43	S. L.	8	M	Nov.	0.85	49.4	Negative	—	Adq.	Neg.	Negative
44	F. S.	9	M	Nov.	0.88	46.5	Negative	—	Adq.	Pos.	Few colds
45	S. L.	11	M	Nov.	0.93	44.1	Negative	—	Adq.	Pos.	Negative
46	C. B.	9	F	Nov.	0.89	35.1	Negative	—	Adq.	Neg.	Negative
47	H. S.	11	M	Nov.	1.08	26.5	Negative	—	Inadq.	Neg.	Negative
48	C. B.	10	M	Nov.	0.93	36.6	Negative	—	Adq.	Neg.	Negative
49	J. C.	10	F	Nov.	0.77	32.6	Negative	—	Adq.	Pos.	Health improved
50	R. M.	9	M	Nov.	1.05	39.9	Positive	Virulent		Neg.	Hoarseness
51	S. P.	10	F	Dec.	1.02	34.4	Negative	—	Inadq.	Pos.	Negative
52	T. V.	9	F	Dec.	0.91	29.4	Negative	—	Adq.	Neg.	One cold
53	A. M.	11	F	Dec.	0.96	39.8	Negative	—	Adq.	Neg.	Negative
54	A. P.	14	M	Dec.	1.02	32.4	Negative	—	Adq.	Neg.	Many colds
55	J. C.	14	M	Dec.	0.69	31.8	Negative	—	Inadq.	Neg.	Slight colds
56	P. A.	13	M	Dec.	0.58	35.1	Positive	—	Inadq.	Neg.	Slight colds
57	W. W.	11	M	Dec.	0.57	18.8	Positive	—	Inadq.	Neg.	Negative
58	H. C.	10	F	Jan.	0.72	25.0	Positive	Non-vir.	Inadq.	Pos.	Negative
59	A. C.	9	F	Jan.	0.60	18.7	Positive	Non-vir.	Inadq.	Neg.	Colds
60	J. N.	8	F	Jan.	0.71	22.5	Negative	—	Adq.	Neg.	Negative
61	A. W.	13	M	Jan.	0.50	26.2	Positive	Non-vir.	Inadq.	Neg.	Negative
62	W. K.	12	M	Jan	0.69	38.2	Negative	—	Inadq.	Neg.	Negative
63	G. R.	13	M	Jan.	0.49	31.5	Positive	Non-vir.	Inadq.	Neg.	Slight colds
64	M. D.	13	F	Jan.	0.76	35.2	Negative	—	Adq.	Pos.	Negative
65	R. D.	10	F	Jan.	0.62	26.9	Negative	—	Adq.	Pos.	Negative
66	J. V.	13	M	Jan.	0.84	35.2	Negative	—	Adq.	Pos.	Negative

TABLE I—CONT'D

NO.	PATIENT	AGE	SEX	MONTH	VIT. C OF BLOOD IN MG.	VIT. C OF TONSIL IN MG.	PRESENCE OF HEM. STREP. IN TONSIL	MOUSE VIRULENCE TEST	DIET VIT. C	DICK TEST	HISTORY OF RESPIRATORY INFECTION SINCE TONSILLECTOMY
67	E. B.	12	M	Jan.	0.68	32.7	Negative	—	Adq.	Pos.	Negative
68	A. L.	14	F	Jan.	0.72	41.6	Negative	—	Inadq.	Pos.	Sore throats, colds
69	V. D.	13	F	Jan.	0.58	32.7	Negative	—	Adq.	Neg.	Negative
70	G. A.	7	F	Feb.	0.76	23.3	Negative	—	Adq.	—	Sore throats, colds
71	V. T.	11	M	Feb.	0.71	26.8	Negative	—	Inadq.	—	Negative
72	L. B.	12	M	Feb.	0.98	31.6	Positive	Non-vir.	Adq.	Neg.	Negative
73	M. R.	10	F	Feb.	1.01	32.5	Negative	—	Adq.	Neg.	Sore throat
74	J. V.	11	M	Feb.	0.75	41.3	Negative	—	Adq.	Pos.	Negative
75	W. R.	11	M	Feb.	0.90	25.5	Negative	—	Adq.	Pos.	Negative
76	B. K.	9	F	Feb.	0.65	29.8	Negative	—	Adq.	Pos.	Negative
77	C. D.	13	M	Feb.	0.94	29.8	Negative	—	Adq.	Pos.	Colds
78	H. G.	9	M	Feb.	0.79	38.3	Positive	Non-vir.	Adq.	Neg.	Negative
79	H. D.	10	F	Feb.	0.85	38.3	Negative	—	Adq.	Neg.	Negative
80	A. P.	12	F	Feb.	0.94	35.8	Negative	—	Adq.	Pos.	Negative
81	I. S.	11	F	Feb.	0.97	48.8	Negative	—	Adq.	Neg.	Negative
82	L. P.	12	F	Feb.	0.93	35.8	Negative	—	Inadq.	Neg.	Negative
83	H. D.	16	M	Feb.	0.87	29.8	Negative	—	Inadq.	Pos.	Negative
84	J. P.	13	M	Feb.	1.05	53.7	Negative	—	Inadq.	Neg.	Negative
85	W. D.	12	M	Feb.	0.94	48.8	Negative	—	Inadq.	Pos.	Bronchitis
86	R. I.	10	M	Feb.	1.05	41.3	Positive	Non-vir.	Inadq.	Neg.	Negative
87	J. M.	13	F	Feb.	1.01	38.3	Negative	—	Adq.	Neg.	Occasional cold
88	F. H.	12	M	Mar.	0.87	41.3	Negative	—	Inadq.	—	Negative
89	E. N.	16	M	Mar.	0.87	41.3	Positive	Non-vir.	Inadq.	—	Negative
90	T. L.	11	F	Mar.	0.97	29.8	Negative	—	Inadq.	—	Negative
91	D. U.	10	M	Mar.	0.84	38.3	Negative	—	Adq.	Neg.	Negative
92	D. M.	9	F	Mar.	0.82	35.8	Positive	Non-vir.	Adq.	—	Colds
93	V. S.	11	F	Mar.	0.89	35.1	Negative	—	Adq.	Neg.	Negative
94	E. M.	12	F	Mar.	0.96	31.3	Negative	—	Inadq.	Neg.	Colds
95	J. M.	11	M	Mar.	0.86	27.3	Negative	—	Adq.	Neg.	Sore throats, colds
96	E. S.	11	M	Mar.	0.96	30.6	Negative	—	Inadq.	Pos.	Negative

about 50 per cent of the children. An inadequate vitamin C intake in the diet was noted in about 40 per cent of the children. With these variations in the findings of apparently healthy children it became im-

Chart 1.—Vitamin C values in milligrams per 100 gm. of tonsillar tissue from 125 pairs of tonsils.

Chart 2.—Vitamin C values in milligrams per 100 c.c. of whole blood from 125 children.

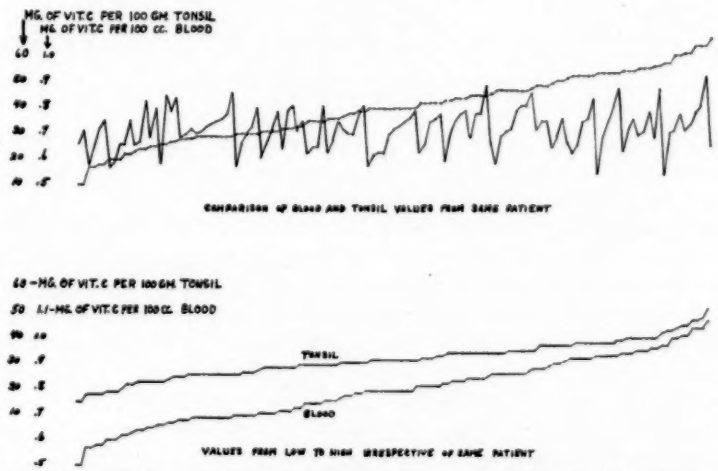

Chart 3.—Vitamin C values in milligrams per 100 c.c. of whole blood and in milligrams per 100 gm. of tonsillar tissue from 125 children.

perative to analyze more carefully the group having high values and those having low values of vitamin C in the blood and in the tonsils.

An analysis of the vitamin C determinations of the blood and the tonsils as noted in the lower graph of Chart 3 shows a parallelism be-

tween the variations in the vitamin C values. Approximately one-third of the children showed low values of vitamin C in the blood and in the tonsils. The middle third represents the average values and the upper third the high values. When, however, the vitamin C values of the blood and the tonsils from the same patient are plotted as is noted in the upper graph of Chart 3, it is obvious that the high and the low values do not always occur in the same patient. In other words, children whose vitamin C blood levels were low frequently showed average or above average amounts of vitamin C in the tonsils. Similarly, patients with high vitamin C values in the tonsils frequently showed low vitamin C values in the blood. There is therefore no constant relationship between the amount of vitamin C of the blood and of the tonsils.

Inasmuch as complete follow-up data were obtained on only ninety-six of the 123 children, this number was divided into three groups, the

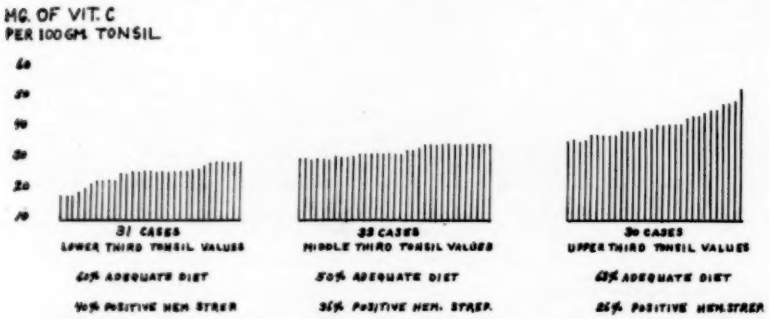

Chart 4.—Incidence of hemolytic streptococci in tonsils of 94 children and the vitamin C intake in their diets.

lower third having the lowest values of vitamin C in the blood and in the tonsils, a middle third which represented the average values, and an upper third with the highest values of vitamin C.

An analysis of Chart 4 shows that in the thirty-one children whose vitamin C content of the tonsils was low, 40 per cent of the tonsils showed evidence of hemolytic streptococci. In the thirty children whose vitamin C content of the tonsils was high, only 26 per cent of the tonsils showed evidence of hemolytic streptococci, while the 33 children in the middle group showed an incidence of 36 per cent infected with hemolytic streptococci. In analyzing the adequacy and inadequacy of the vitamin C in the diet, it was noted that no great difference was found in the three groups.

A similar analysis of Chart 5 shows that in the lower third of vitamin C blood values, 55 per cent of the tonsils showed evidence of hemolytic streptococci while in the upper third only 10 per cent of the tonsils showed evidence of streptococci infection. The adequacy of the vitamin C in the diet was noted with equal frequency in all three groups.

It appears from these observations that apparently healthy children, some of whom are receiving an adequate ration of vitamin C in their diet while others are not, have a considerable range of storage of vitamin C both in the blood and in the tonsillar tissue. There is a significant difference in the percentage of hemolytic streptococci found in the tonsils in these children. Based on the vitamin C content of the blood it is evident that hemolytic streptococci were found five times as often where the blood values were 0.7 mg. per cent or less, than when the blood values were 0.85 mg. per cent or more.

In order to more accurately determine if there is any significant difference in the incidence of hemolytic streptococci in the tonsils when there is a variation in the vitamin C of the blood and the tonsils further

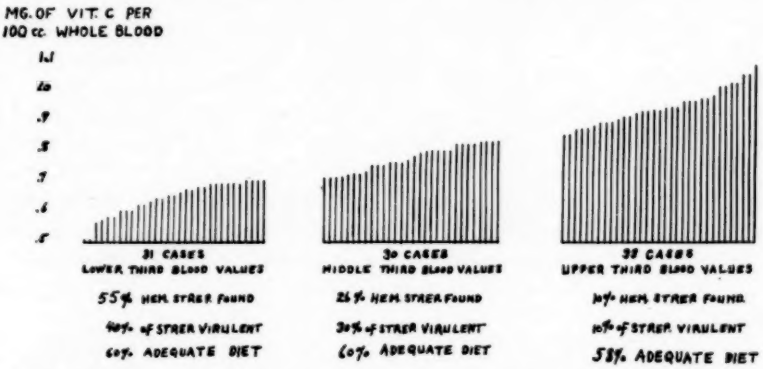

Chart 5.—Incidence of hemolytic streptococci and their virulence found in the tonsils of 94 children, based upon the vitamin C content of the blood of these children.

analyses were made. The entire group of 123 children was utilized. The mean values and the reliability of this mean were ascertained utilizing σ, the standard deviation; $\frac{100\ \sigma}{m}$, the coefficient of variability, and ϵ, the probable error of the mean.

TABLE II

COMPARISON OF THE GROUPS WITH AND WITHOUT HEMOLYTIC STREPTOCOCCI IN THE TONSILS

VITAMIN C. OF TONSILS	NUMBER	MEAN	σ	ϵ	$\frac{100\ \sigma}{m}$
No streptococci	77	34.32	7.78	0.604	22.7
Streptococci	46	30.44	7.49	0.754	24.6
Difference of means: 3.88 ± 0.965 – significant.					
VITAMIN C. OF BLOOD	NUMBER	MEAN	σ	ϵ	$\frac{100\ \sigma}{m}$
No streptococci	77	0.8201	0.1328	0.0103	16.2
Streptococci	46	0.7544	0.1445	0.01452	19.1
Difference of means: 0.0657 ± 0.0178 – significant.					

It appears from these calculations that the vitamin C content of the blood and of the tonsil is significantly lower in children whose tonsils contain hemolytic streptococci than in those whose tonsils do not contain hemolytic streptococci.

It is also possible to divide the observations into four groups: Those with vitamin C of blood and of tonsils both below the mean; those with vitamin C of blood and of tonsils both above the mean; those with vitamin C of blood above and vitamin C of tonsils below the mean; and those with vitamin C of blood below and vitamin C of tonsils above the mean. When this is done for the groups with and for those without streptococci in the tonsils, the diagram of Fig. 1 results.

PER CENT INFECTED

Blood		
↑ high	37.7	21.1
low	53.2	41.7
	low	high

→ tonsils

Also, the correlation coefficient, r, between the vitamin C of the tonsils and the vitamin C of the blood was determined: In cases without streptococci in the tonsil, $r = 0.197 \pm 0.0739$; in cases with streptococci in the tonsil, $r = -0.0217 \pm 0.0995$. Only the former is significant.

In the case of determining the adequacy of vitamin C in the diet, it was found difficult to know when a child was receiving an inadequate amount. Inasmuch as the chief source for these children is from the citrus fruits, tomato juice and pineapple juice, the determinations were made on the parents' response as to the daily or periodic ingestion of one or more of these sources. No accurate information was obtained as to the diet of these children other than that of the fruit or vegetable juices mentioned. Based on this incomplete dietary information, no relationship could be found between low vitamin C values and an adequate vitamin C intake.

The significance of finding hemolytic streptococci in the tonsils is not clear. In the majority of the children in whom the organisms were found, no recognizable symptoms were present. An effort was made to determine the degree of virulence of these streptococci. Intraperitoneal injections of mice were made. Using control mice it was felt that some estimate of the virulence of the streptococci could be determined. An analysis of the virulence tests shows that 40 per cent of the streptococci found in the tonsils of children that had the lowest values of vitamin C were virulent; 30 per cent were virulent where the

vitamin C values were average and only 10 per cent were virulent where the vitamin C values were above average. These findings suggest that not only are streptococci less likely to be found in tonsils where the blood values are high but if they are present, they are seldom virulent.

A clinical history of the children was tabulated to determine if the children harboring streptococci in the tonsils were more liable to upper respiratory infections than those whose tonsils did not show the presence of hemolytic streptococci. A few of the 96 children had been operated on for nine months, but most of them for less than six months. Such a period is obviously too short to observe the clinical course of these children. A number of the children have had attacks of sore throat, adenitis, and ear infections. Most of them showed streptococci in the tonsils. It is obviously unfair to pass any opinion on so few cases observed over such a short period of time.

Dick tests were performed on all of these children to determine if a positive Dick test was present more frequently in children with hemolytic streptococci in the tonsils and with low vitamin C values in the blood. No significant relationship could be found between a positive Dick test and the presence or absence of hemolytic streptococci in the tonsils, nor was any relationship noted in the cases of low vitamin C content of the blood in these children.

DISCUSSION

The various clinical reports on the influence of vitamin C on infections, notably rheumatic fever and tuberculosis, suggest that there might be some inhibitory influence of ascorbic acid on certain organisms. Before studying this relationship in the human body a series of experiments was undertaken to show the effect of vitamin C on certain organisms in vitro. The inhibitory effect of various dilutions of ascorbic acid was studied in the case of hemolytic streptococci, pneumococci, staphylococci, typhoid bacilli, coli bacilli, pertussis bacilli, and influenzae bacilli. It was found that the groups of virulent hemolytic streptococci were completely inhibited in twenty-one consecutive experiments, while in all instances the controls grew freely. Similar results were obtained using pneumococci and pertussis bacilli and influenzae bacilli. In the case of the coli bacillus, typhoid bacillus and staphylococcus, no inhibition was obtained. To obtain these results it was necessary to maintain a pH of from 3.4 to 4 with a solution of ascorbic acid of 1-100. A less acid solution did not completely inhibit these organisms. Other acids such as hydrochloric acid and acetic acid in the same dilution were also employed. They rarely inhibited the growth of hemolytic streptococci in vitro. These experiments suggest that ascorbic acid in adequate amounts with a pH of 4 exercised a definite inhibitory effect on certain organisms, especially hemolytic streptococci. A series of

experiments was also conducted in vivo to determine if various amounts of ascorbic acid protected laboratory mice from hemolytic streptococci infections. The experiments in mice that received intraperitoneal injections of a virulent strain of hemolytic streptococci were less conclusive, but a considerable number escaped death where vitamin C was injected simultaneously with the lethal dose of hemolytic streptococci.

These observations prepared us for a study of the hemolytic streptococci found in the substance of the tonsils of children. It was not surprising, therefore, to find a higher incidence of streptococci in the tonsils of such children who showed low values of vitamin C or ascorbic acid in the blood.

If we can assume, as has been suggested by some authors, notably Abt, Farmer and Epstein,[4] that the vitamin C content of the blood is an index to the amount of vitamin C stored in the tissues, there should be some relationship to the ability of hemolytic streptococci to live in tissues where varying amounts of vitamin C are found. The tonsils were known to be well supplied with vitamin C, as has been shown by Clayton and Keith.[6] The amount of vitamin C found in the tonsils compares favorably with the amounts found in the adrenals and in the liver. Frequently, as is shown in our studies, the vitamin C content of the blood and of the tonsils bears a parallel relationship, though there are some variations which cannot be explained. The incidence of hemolytic streptococci in the freshly operated tonsils is definitely higher in the individual in whom the content of the vitamin C is low in the blood and in the tonsils, and it is low in such children where the vitamin C of the blood and the tonsils registers higher values. Inasmuch as the study of the streptococci was made from operated tonsils, no further study could be made of the lymphoid tissue even after the child had been saturated with vitamin C. Such studies would be helpful if an increase in the blood values of vitamin C would bring about a diminution in the number of hemolytic streptococci in the tonsils. The evidence at hand suggests that an adequate amount of vitamin C in the blood influences the incidence of hemolytic streptococci found in the tonsils. However, it is also possible that infection of the tonsil causes a lowering of the vitamin C content. Insufficient evidence is at hand to venture the opinion that when the amount of vitamin C falls below a certain level in the blood the individual is more liable to become infected with hemolytic streptococci. Other factors undoubtedly play a part in this mechanism.

The amount of vitamin C found in human blood is probably determined by the amount of this vitamin obtainable from certain foods. The daily ingestion of a reasonable amount of orange juice does not assure a high level of vitamin C in the blood in all instances according to the data obtained in this group of children. On the other hand, where

generous amounts of vitamin C are taken daily in the form of orange juice, tomato juice, or pineapple juice, the vitamin C blood levels are uniformly high or in the average zone. It would seem therefore that the metabolism of vitamin C varies in children. This is known to be the case in the presence of infection and may be so in the absence of infection. The definite evidence of finding fewer hemolytic streptococci in the tonsils of children with average or better than average vitamin C content suggests an inhibitory relationship in the human body. Certainly from the clinical point of view it is desirable to supply the children with more than the minimum amount of vitamin C in their diets.

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16 NORTH GOODMAN STREET

VITAMIN C IN TUBERCULOSIS

The Effect of Supplementary Synthetic Vitamin C on the Urinary Output of This Vitamin by Tuberculous Children

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In A recent publication[1] the authors observed the constant occurrence of hypovitaminosis C in active tuberculosis in children, determined by the subnormal excretion of the vitamin in the urine. In the study of thirty-seven cases in the Buffalo City Hospital an average excretion of 5.7 mg. per twenty-four hours was noted (reducing power as determined by the dichlorophenol indophenol method) on a daily ration of 55 to 65 mg. of vitamin C, whereas twenty-five normal, healthy children on approximately the same diet averaged 29.2 mg. per twenty-four hours. The present study was conducted to determine the approximate number of milligrams of synthetic vitamin C required to establish and maintain normal excretory levels of the vitamin in these tuberculous children.

METHOD

A group of ten tuberculous children taken from the larger group previously reported was selected. The diet for these children, considered to be high in vitamin C, contained approximately 55 to 65 mg. daily. Following a period to determine the basic vitamin C elimination level, 50 mg. of synthetic vitamin C in tablet form were added to the daily diet until normal excretory levels were established and maintained. A single case was then observed daily after discontinuance of the added vitamin, the diet returning to the basic intake of 55 to 65 mg. daily. Also, the urinary vitamin C output of the other nine patients was determined two weeks after discontinuance.

As a control the basic vitamin C elimination level of six normal, healthy children in middle-class American homes was established. As far as could be ascertained these children had an average vitamin C intake comparable to that of the tuberculous group, namely 55 to 65 mg. daily. Subsequently the diet of this group was also augmented by the same 50 mg. synthetic vitamin C tablet until the maximal increase in urinary output was obtained. The supplementary vitamin was then discontinued, and the results noted. The chemical technique used for the determination of vitamin C in urine was a modification of the dichlorophenol indophenol method of Harris and Ray, as previously described.[1]

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CLINICAL MATERIAL

All ten of the tuberculous children had pulmonary involvement, cavitation being present in seven patients and a positive sputum in six.

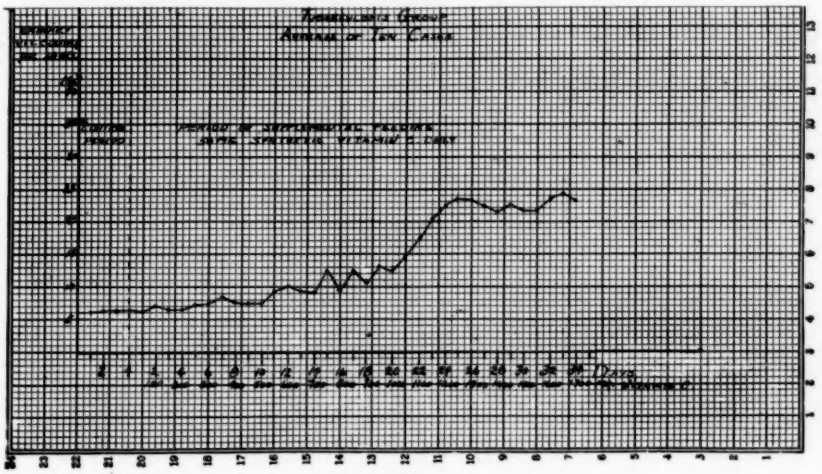

Fig. 1A.

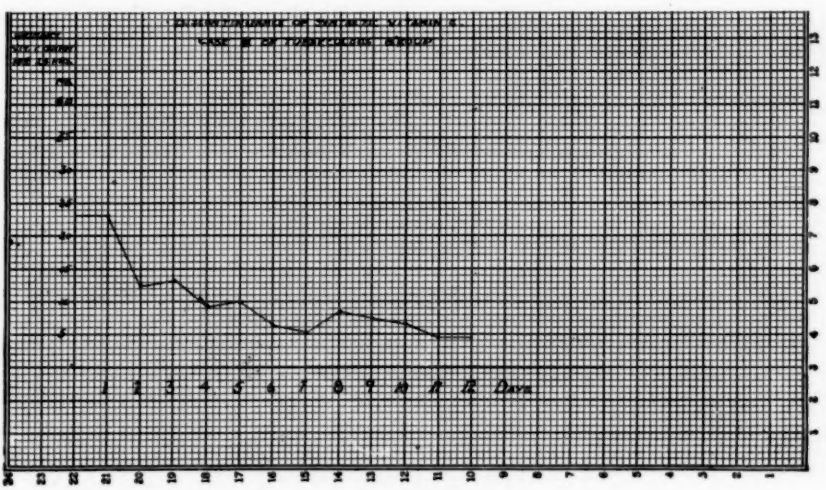

Fig. 1B.

Two showed associated involvement of the spine. The nutrition was considered poor in two cases and fair in eight. Eight were bed patients, and the other two were partially ambulatory.

TABLE I

TUBERCULOUS GROUP

DAYS	MG. FED	MILLIGRAMS EXCRETED PER 24 HOURS										AVERAGE
		CASE 1	CASE 2	CASE 3	CASE 4	CASE 5	CASE 6	CASE 7	CASE 8	CASE 9	CASE 10	
Control Period												
1		0.5	1.9	6.8	6.7	8.0	5.5	5.5	7.1	6.1	8.1	6.12
2		5.5	2.1	9.7	2.4	10.1	6.5	6.5	7.2	7.2	5.1	6.23
3		7.2	9.7	6.5	2.7	6.9	4.5	6.2	7.4	3.4	8.3	6.28
4		6.4	6.8	9.5	6.6	6.5	6.8	5.3	6.1	5.5	7.2	6.67
Period of Supplementary Feeding of 50 Mg. Daily of Synthetic Vitamin C												
1	50	8.1	5.2	7.5	5.2	5.6	6.4	6.8	6.0	6.5	6.1	6.34
2	100	5.8	7.4	8.2	6.5	6.5	7.2	7.2	7.5	7.9	8.5	7.07
3	150	6.4	6.8	9.5	5.2	8.4	5.9	5.9	8.2	8.3	3.8	6.84
4	200	7.2	5.2	6.5	8.4	3.9	8.7	7.5	5.5	6.4	9.5	6.88
5	250	6.1	3.1	5.6	9.5	8.5	9.2	8.2	8.3	8.3	6.8	7.36
6	300	6.5	4.8	9.5	8.6	4.2	6.4	9.1	9.1	9.4	7.2	7.48
7	350	3.0	8.5	10.1	6.9	6.5	10.1	6.8	7.2	9.5	9.3	8.79
8	400	6.8	9.2	8.2	7.8	10.4	9.3	7.5	6.8	8.4	4.9	7.93
9	450	7.5	6.5	5.4	6.5	10.1	8.4	8.2	6.5	3.9	6.8	7.98
10	500	5.5	8.8	6.9	5.2	9.5	6.1	6.8	7.5	9.5	7.1	7.29
11	550	8.3	7.2	6.3	9.0	15.8*	6.8	7.9	9.1	5.5	8.1	9.40
12	600	6.4	10.1	10.5	8.9	24.7	7.3	9.5	9.8	6.2	9.0	10.24
13	650	5.4	8.5	13.2	7.0	20.5	8.0	8.8	8.2	5.9	10.1	9.56
14	700	6.5	9.1	12.1	6.6	18.7	8.2	6.8	7.4	8.7	8.2	9.23
15	750	7.5	14.4	15.0	6.5	32.2	8.4	8.8	10.4	8.7	11.1	12.30
16	800	6.3	10.5	10.0	8.7	25.2	9.6	6.9	6.9	6.3	8.3	9.82
17	850	12.5*	24.0*	12.0	14.3	20.5	8.2	7.4	8.2	8.1	9.1	12.43
18	900	15.0	18.5	9.4	7.5	21.2	6.5	7.5	6.4	7.7	7.2	10.69
19	950	21.4	20.5	12.0	9.5	25.5	8.5	10.1	5.9	10.5	6.8	13.13
20	1000	22.4	19.5	16.0*	10.1	19.5	6.2	9.4	8.5	8.5	6.2	12.63
21	1050	25.5	17.5	18.0	10.8	25.2	9.5	11.5	10.1	12.5	9.2	14.98
22	1100	24.3	16.0	21.2	12.5	26.5	10.1	16.9*	19.5*	13.0	12.9	17.29
23	1150	21.4	20.1	20.0	15.5*	28.7	12.5	25.5	29.5	15.0*	18.1*	20.63
24	1200	28.7	16.8	72.5	20.1	30.1	15.5*	29.4	18.2	18.0	24.5	22.38
25	1250	27.2	18.0	20.5	18.2	27.2	17.5	35.5	28.5	21.5	19.9	23.40
26	1300	23.3	24.0	24.7	22.5	24.3	16.5	27.2	25.3	27.0	17.8	23.25
27	1350	19.5	18.7	17.0	19.5	21.2	20.4	25.2	30.1	18.5	18.5	22.86
28	1400	22.4	17.5	15.0	22.5	19.4	21.3	28.5	26.1	19.0	20.5	21.22
29	1450	25.4	21.2	21.0	19.6	30.5	18.7	30.1	20.5	16.5	23.8	22.73
30	1500	22.0	21.5	22.4	18.6	23.0	16.4	28.5	22.5	26.8	17.5	21.92
31	1550	25.2	27.6	28.3	21.5	19.5	19.3	25.2	19.8	13.2	19.8	21.94
32	1600	28.4	25.5	24.2	22.0	27.8	23.5	26.1	16.8	19.5	24.2	23.80
33	1650	21.5	27.5	25.0	27.0	20.4	20.4	22.2	24.8	23.5	19.8	24.41
34	1700	27.2	22.8	21.0	25.0	22.4	24.3	20.0	21.3	28.7	20.0	23.27

*Indicates day of significant rise.

RESULTS

In the tuberculous children the basic excretion on the diet of 55 to 65 mg. was 6.4 mg. per twenty-four hours as determined over a period of four days (Table I and Fig. 1*A*). In only one instance a result was found more than 10 mg. (10.1 mg. in Case 5 on the second day). Upon addition of the synthetic vitamin to the diet, an average total of 750 mg. over a period of fifteen days produced a rise in urinary output to levels slightly over 10 mg. per twenty-four hours and a total of 1,050 mg. in twenty-one days to 15 mg. per twenty-four hours. On the twenty-fourth day, after 1,200 mg. had been given, the average excretion had risen to 23 mg. per twenty-four hours. Continued feeding for another ten-day period showed a maintenance of this latter level, but there was no further rise. A typical case (Case 8) was studied after discontinuance of the supplementary vitamin. As shown in Fig. 1*B*, basic levels of 6 to 7 mg. per twenty-four hours occurred on the sixth day and were maintained for the remainder of the study, that is, eight more days. In only one instance (Case 5) was there considerable variation from the average.

TABLE II

NORMAL CONTROL GROUP

DAYS	MILLIGRAMS EXCRETED PER 24 HOURS						AVERAGE
	CASE 1	CASE 2	CASE 3	CASE 4	CASE 5	CASE 6	
Control Period							
1	54.0	36.0	18.5	37.0	30.5	31.5	34.6
2	58.0	24.0	20.5	33.0	31.0	34.0	34.6
3	41.5	31.0	41.0	37.0	24.5	21.5	33.4
4	40.5	36.0	27.0	39.0	28.0	40.0	35.1
5	28.0	35.0	27.5	32.0	28.5	30.0	30.2
Period of Supplemental Feeding of 50 Mg. of Synthetic Vitamin C							
1	49.5	39.0	44.0	44.0	42.0	35.0	42.3
2	79.0	60.0	70.0	68.0	64.0	82.0	70.5
3	84.0	68.0	68.0	79.0	81.0	78.0	76.4
4	92.0	77.0	72.0	84.0	71.0	69.0	77.5
5	83.0	74.0	65.0	80.0	82.0	75.0	77.5
6	74.0	80.0	69.0	72.0	73.0	69.0	73.0
Period of Discontinuance of Synthetic Vitamin C							
1	64.0	58.0	50.0	59.0	68.0	54.0	58.8
2	56.0	43.5	39.0	35.0	38.0	24.0	35.9
3	30.0	42.0	32.5	32.0	38.0	30.0	34.2
4	35.0	38.0	36.0	37.0	49.0	28.0	37.2
5	38.0	30.0	29.0	30.0	25.0	35.0	31.2
6	38.0	24.0	30.0	35.0	31.0	32.0	31.7

In this case 600 mg. over a period of twelve days were sufficient to produce an output of 24 mg. per twenty-four hours, while the highest excretion was 32 mg. per twenty-four hours. This was clinically the least severe of all of the cases. In the other nine patients, all with severe involvement, little variation in response to supplementary feeding was noted.

In the healthy control patients, on approximately the same basic diet, a five-day preliminary examination to establish a base line (Fig. 2 and

*Indicates day of significant rise.

Table II) showed an average excretory level of 30 to 35 mg. per twenty-four hours. Upon supplementary feeding of 50 mg. of the same synthetic vitamin daily, a sharp increase promptly resulted, averaging 70 mg. per twenty-four hours on the second day after a total of 100 mg. had been taken. The maximum of 77.5 mg. per twenty-four hours was noted on the fourth day, after which time continued feeding for two more days revealed a maintenance but no further increase in the excretion of vitamin C. Upon discontinuance of the supplementary vitamin, the urinary output fell rapidly, the previous basic level of 30 to 35 mg. per twenty-four hours being reached on the third day.

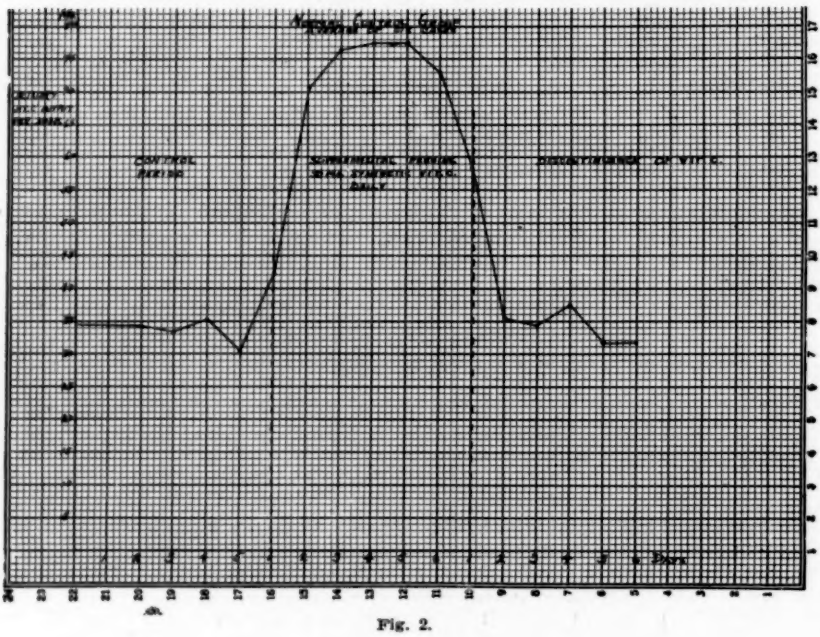

Fig. 2.

DISCUSSION

A comparison between the tuberculous and the control groups revealed certain significant differences. In the first place, the average basic level of the urinary excretion of vitamin C in the two groups varied considerably. The tuberculous group consistently excreted less than 10 mg. per twenty-four hours, the average of 6.4 mg. per twenty-four hours being below the accepted minimal normal levels of from 10 to 15 mg. per twenty-four hours.[2] On the other hand, the control groups of healthy children, with an average of 30 to 35 mg. per twenty-four hours, was definitely above this minimal normal level. As far as could be ascertained, the vitamin C intake of this latter group was approximately

similar to that of the tuberculous group, showing that such a diet in a healthy child is adequate, but in one with a chronic infection, such as existed in the tuberculous group, it was insufficient.

Additional corroboration of the fact that the basic diet was adequate in the healthy children and inadequate in the tuberculous ones was offered by the results obtained from supplementary feeding of the vitamin. Additional feeding to the normal group resulted in a prompt rise of the vitamin excretion, with a maximal recovery of 84 per cent of the added vitamin. This would point to a "spilling over" of the excess vitamin into the urine, vitamin C being generally considered a threshold substance,[3] and would indicate saturation of the tissues. On the other hand, supplementary feeding did not cause a comparable rise in the tuberculous children. An average of 750 mg. in fifteen days was necessary to produce an excretion of 10 mg. per twenty-four hours and 1,050 mg. in twenty-one days for a level of 15 mg. per twenty-four hours. Thus, hypovitaminosis may be said to have existed in this group. Furthermore, assuming that vitamin C saturation of the body tissues was reached when the urinary excretion varied between 10 and 15 mg. per twenty-four hours, saturation could then be said to have been present in the tuberculous group somewhere between the fifteenth and twenty-first days. The average amount of vitamin C necessary to produce saturation could also be placed somewhere between 750 and 1,050 mg. Direct proof of saturation at this latter time might have been obtained by recovery, in high percentage similar to that found in the normal group, of an additional dose of vitamin C, for example, 100 mg. Unfortunately, this procedure was not performed. However, indirect proof was afforded by the comparatively sharp increase from 15 mg. per twenty-four hours to 23 mg. per twenty-four hours, which occurred from the twenty-first to the twenty-fourth day following continuation of the supplementary feeding. The less spectacular increase in the urinary excretion in the tuberculous group at this time, when compared to the normal group, could be explained by the hypothesis that nearly all of the supplementary vitamin was required for the maintenance of saturation. Further proof would seem afforded by the fact that continued feeding for another ten-day period (twenty-fourth to thirty-fourth day) showed no increase in the excretory level, indicating that the combined total of vitamin, namely 105 to 115 mg., was only slightly above the amount required for the maintenance of saturation in the tuberculous children.

Only one patient (Case 8) was studied following withdrawal of the supplementary vitamin. This patient showed a decline in excretion to the previous basic level, that is, 6 mg. per twenty-four hours in seven days. A check of the other nine patients, two weeks after discontinuance of supplementary vitamin, showed a similar return to the same basic level. This would seem additional proof of unsaturation.

As already mentioned, only one patient (Case 5) showed much variation from the average, requiring only 600 mg. per twenty-four hours to reach a urinary output of 24 mg. per twenty-four hours, while the highest excretion was 32 mg. per twenty-four hours. This patient showed clinically the least involvement of any of the tuberculous children. The other nine patients clinically exhibited a greater degree of involvement, but no significant variation in severity in any given case could be noted. On such a disproportionate division it is perhaps unwise to draw conclusions, but it would appear that increased demand for vitamin C was in direct relation to the severity of the tuberculous process. No attempt, in this study, has been made to evaluate the therapeutic effect of the production of vitamin C saturation in the tuberculous group because of the comparatively short period for observation. However, reports are to be noted in the literature[4] in which clinical improvement in the tuberculous process has been noted following augmented vitamin C intake. This would seem logical, as the tendency to hypovitaminosis in active tuberculosis appears pronounced.

SUMMARY AND CONCLUSIONS

A study comparing the vitamin C urinary excretion of a group of tuberculous and normal children, both on approximately the same basic vitamin C diet, that is, 55 to 65 mg. daily, was made, after which 50 mg. of synthetic vitamin C was added to the daily diet. An immediate rise was noted in the normal group, whereas the tuberculous group, in whom the average basic excretion was 6.4 mg. per twenty-four hours, required an average of 750 mg. in fifteen days to produce a rise in excretion to 10 mg. per twenty-four hours. The maximal output (23 mg. per twenty-four hours) was obtained on the twenty-fourth day after 1,200 mg. had been ingested. Subsequent feeding produced no further increase. Upon discontinuance of the added vitamin, the excretion of the tuberculous group promptly fell to the previous subnormal levels. This study points to hypovitaminosis C in active tuberculosis and suggests increased vitamin C intake as a therapeutic measure.

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THE EVALUATION OF SEROLOGIC TESTS FOR CONGENITAL SYPHILIS

With Special Reference to the Neonatal Period

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THE recognition of congenital syphilis in the neonatal period often presents formidable difficulties. Definite clinical signs of syphilitic infection at birth are relatively rare. The longer the interval since the mother's infection (Kassowitz' law) and the more specific treatment she has received, the greater are her chances of giving birth to an apparently healthy infant. Treatment that is inadequate[1] may fail to protect the offspring and yet be sufficient to postpone and mask signs of infection in the newborn infant.

Some clinics rely, during the early months of infancy, on x-ray pictures of the long bones, but these often fail to reveal unequivocal signs of infection. McKelvey and Turner[2] found 69.3 per cent of the syphilitic infants in their series negative roentgenologically. If it were feasible to obtain films at frequent intervals, the number of cases of congenital syphilis discovered by this method undoubtedly would be higher. Pathognomonic changes shown in the films of the long bones of infants[3, 4] afford a sound basis for a positive diagnosis and are especially valuable in confirming a diagnosis based on clinical or serologic evidence. However, recent studies by Christie[5] point out pitfalls in the interpretation of films of the long bones.

Some of the traditional views regarding the reliability of serologic tests for syphilis in the newborn infant are in need of revision because, in many instances, these views are based on the results of tests which were relatively inefficient. True positive reactions were missed, and false positive reactions were relatively frequent. The recent evaluation of serodiagnostic tests for syphilis conducted under the auspices of the U. S. Public Health Service,[6] has brought into striking relief the wide differences in the efficiency of the participating laboratories.

A single qualitative blood test in the newborn infant, whether positive or negative, is by itself no criterion of the presence or absence of syphilitic infection. Recent workers[7, 8, 9] have suggested that a reaction in the blood of the newborn infant, which is quantitatively of higher titer than that of the mother, indicates actual syphilitic infection of the infant. Additional experience is desirable in order to confirm this impression. Even in the presence of a transmitted infection, many fac-

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tors, such as the immunologic immaturity[10, 11] of the infant, late intrauterine infection, or treatment of the mother, may delay the production of sufficient syphilitic reagins in the blood of the newborn infant to be demonstrable by even the more sensitive tests. On the other hand, enough specific reagins may be transmitted from the serologically positive mother to give an uninfected infant a positive blood test (Fildes' law). The phenomenon of the passive transmission of antibodies and reagins in utero[12] is not unusual. To call this reaction a "false positive" is doing the test an injustice in most instances. A specific serologic test reports the presence or absence of syphilitic reagins and not the presence or absence of *Treponema pallidum*.

The importance of not making a diagnosis of congenital syphilis at birth on the basis of a single positive blood test is being recognized by an increasing number of physicians. Although the incidence of congenital syphilis is probably greater among the seropositive newborn infants than among the seronegative infants,[13] one would not be justified in making a diagnosis nor in starting treatment on the basis of this probability alone. Cregor and Dalton[14] found that if all the infants of syphilitic mothers in their series were treated, 91 per cent would be treated needlessly; and if all the newborn infants with a positive Wassermann reaction were treated, 69 per cent would be subjected to this procedure needlessly.

Using the Wassermann (complement fixation) reaction, Dunham,[7] Faber and Black,[8] and Christie[9] have titrated the specific serologic reactions in newborn infants over a period of weeks and months. According to them, a falling titer of syphilitic reagins presumably indicates a passively transferred reaction, whereas a reaction that is stronger than that of the mother at the time of delivery or one that increases progressively in titer indicates congenital syphilis. Christie extended the period of observation beyond that of Faber and Black and thereby was able to demonstrate that the mere decline or disappearance of a "pseudopositive" reaction does not prove that the infant has escaped the disease. A true positive reaction may be late in developing even though congenital infection is present. This time factor has been taken into account in evaluating the results of the neonatal serologic reactions in this study.

The purpose of this study was to follow the course of the serologic reactions of a series of infants born in 1935 and 1936 of syphilitic mothers. These infants were born in the Boston Lying-in Hospital, with the exception of a pair of twins who were admitted to the hospital soon after birth because of their small size. Although not all the infants of these mothers were brought to the attention of the investigators, eventually fifty-six were available for the survey. The first forty infants had been delivered at least twelve months, the next twelve infants from six to twelve months, and the last four from four to six

months before the study closed. The final statistics were obtained May 1, 1937, four months after the last infant in the series was born.

The infants were given a careful physical examination at birth and on discharge from the maternity hospital, through the cooperation of the staff of the Boston Lying-in Hospital and the staff of the Infants' and Children's Hospitals. An attempt was made to secure a regular Hinton test for syphilis and x-ray films of the long bones within the first week after birth. Occasionally a cord blood specimen was sent to the Wassermann Laboratory for a Hinton and a Wassermann test. Placentas were examined by a competent pathologist, but no scrapings were made of the umbilical veins for *Treponema pallidum*.

Previous studies on the titration of the strength of the early positive reaction of infants born of syphilitic mothers[7, 8, 9] employed serial dilutions of serum obtained by venepuncture of the infant. In this study the strength of the serologic reactions of the infants was determined by the capillary Davies-Hinton test,[15] which is a micromodification of the Hinton flocculation test. This microtest requires merely 0.05 c.c. of serum, and the blood specimens were obtained by puncture of the infants' great toes. In an evaluation series conducted under the auspices of the U. S. Public Health Service in 1935,[6] this test attained a sensitivity of 91.9 per cent and a specificity* of 100 per cent. In the same series, the Hinton control test was rated 88.8 per cent sensitive, the Kahn control test 75.5 per cent, the Kline diagnostic control 88.8 per cent (and 99 per cent specific), and the Kolmer (complement fixation) Wassermann control 59 per cent sensitive. Because of the small amount of blood necessary for the test and the relative ease with which each specimen was obtained, it appeared feasible to take several samples of blood during the neonatal period. In most cases a similar test was made of the mother's capillary blood within a few days after delivery.

Although it is possible to titrate the strength of the capillary Hinton reaction by dilutions of the serum with Hinton-negative nonsyphilitic serum, the simpler routine capillary method was adopted. In this test the strength of the reaction is estimated in a mixture of equal parts of inactivated serum and Hinton antigen or indicator.† Thus no special dilutions were necessary. Experience enables one to estimate fairly

TABLE I

REACTION AT THE MENISCUS	RATING
Firm, cohesive disc or cone	4 plus
Disc easily broken into large and small aggregates	3 plus
Medium-sized, discrete aggregates	2 plus
Small, definite aggregates	1 plus
Negative	-

*Absence of false positive reactions.

†In actual practice a tube containing a mixture of one part serum to five parts Hinton antigen was also set up.

consistently the strength of the reaction at the meniscus in the tube after centrifugation. Designations which were used are given in Table I.

Ten newborn infants, aged 1 to 10 days, whose mothers had negative Hinton tests and were considered free from syphilis, served as controls. Their capillary Davies-Hinton tests were negative.

Congenital syphilis was detected in only one infant of the fifty-six in the series during the neonatal period. The baby was placed under treatment immediately and is now in excellent condition. The others were directed, upon discharge from the maternity hospital, to one of the Boston clinics or to their private physicians for suitable follow-up examinations.[16]

The plan adopted at the Infants' and Children's Hospitals was to examine each infant at the approximate ages of 6 weeks, 3 months, and 1 year. In special cases the intervals between visits were shortened. At each examination a blood specimen was taken for either a regular Hinton or a capillary Davies-Hinton test. X-ray films were ordered when serious doubt arose as to the condition of the child. Tables II, III, and IV summarize the results of the study. In spite of special efforts to secure the return of all the infants for periodic examinations, only twenty-two (including two that died of pneumonia) out of the forty who were born a year or more before the final statistics were obtained were considered to have satisfactory follow-up records. As the result of the first examination after discharge from the maternity hospital, a second infant (No. 55) was found to have syphilis.

Further studies with careful observation over a period of at least one year are necessary in order to determine the minimum length of time during which infants born of syphilitic mothers should receive periodic examinations in order to rule out the possibility of congenital infection. In this way only can the prognostic significance of early serologic tests be determined accurately. Most infants with congenital syphilis will probably develop positive blood tests by one of the more sensitive methods within four months after birth.[5] Infants and children with evident signs of syphilis are almost all serologically positive, according to Jeans and Cooke.[17] In order to rule out infection that is slow in developing it would seem that, in our present state of knowledge, infants of syphilitic mothers should be kept under observation for at least one year. At the end of this time they should be clinically and serologically free from all evidence of the disease.

It may be noted that the titer of the second specimen was sometimes higher than that of the first, particularly if the first specimen was taken shortly after birth. The cause of this preliminary rise is not clear. Some of these infants were moderately dehydrated at the time of the first test and had high hematocrit readings and icteric serum. In the single case of congenital syphilis detected during the first two weeks

TABLE II

INFANTS BORN CONSECUTIVELY AT LEAST ONE YEAR BEFORE CONCLUSION OF THE STUDY

NEONATAL BLOOD TESTS POSITIVE

	NEONATAL PERIOD														FOLLOW-UP PERIOD						MOTHER		
	CAPILLARY HINTON TESTS																						
SERIAL NUMBER	RESULT	DAY	RESULT	DAY	RESULT	DAY	RESULT	DAY	CORD HINTON	HINTON TEST	DAY	WASSERMANN	DAY	X-RAY OF L.B.	DAY	LAST POSITIVE	BLOOD TEST	FIRST NEGATIVE	BLOOD TEST	LAST NEGATIVE	BLOOD TEST	X-RAY NEGATIVE	SYPHILIS	CAPILLARY HINTON	REMARKS
122	-	3	-	7	+	11	+++	17						-	3	3m	*CH	7m	H	14m	CH	3m	A		Normal infant
7	++++	9	++++	11	+++	14								-	2								A	++++	No follow-up
13	++	9	++++	12						Pos.	12			+	11	3m	HW	8m	H	18m	H		A	++++	Congenital syphilis
12	++	1	+	4	-	5	-	12		-	5			-	1	4d	CH	5d	CH	1m	CH	1m	C	+++	Incomplete follow-up†
35	++	2	++	4	+	10	-	13		-	5			-	2	3m	H						A	++++	Congenital syphilis
21	++++	2												-	4	40d	*CH	8m	CH	18m	CH		A	++++	Normal infant (Col.)†
39	++	1	+++	2	+++	5	+	9		-	11	-	11			9d	CH	4m	CH	13m	CH		C	++++	Normal infant
J	+	3	+	4	-	7				-	3			-	3	4d	CH	7d	CH	8m	CH		A	+++	Incomplete follow-up
59	++	1	-	3	-	18			-					-	1	2d	CH	3d	CH	12m	CH		A	++++	Normal infant (Col.)
46	++	3	-	5					-	-	2	-	2	-	2	3d	CH	5d	CH	9m	H		A		Incomplete follow-up
71	+++	1	++++	2	+++	6	++	10		-	2	-	2	-	2	10d	CH	3m	H	3m	H	3m	C	++++	Died, pneumonia†
54	++	1	-	3					-	-	2			-	2	1d	CH	3d	CH	13m	CH		C?	++++	Normal infant
55	++	2	-	9						-	2	-	2	-	2	2d	CH	9d	CH	12m	CH	2m	C	+++	Normal infant
68	++	2	++++	6	-	9				-	10	-	2	-	5	6d	CH	9d	CH	14m	CH		C	++++	Normal infant
76	+	1	-	4	+	11						-	5	-	1	11d	CH						A	++++	No follow-up
I	++	1	++	5	+	8				-	1	-	1	-	2	8d	CH	50d	CH	6m	CH		A	++++	Incomplete follow-up
58	++	1	+++	7	-	12			-	-	2	-	2	-	2	7d	CH	12d	CH	5m	HW		A	++++	Incomplete follow-up
75	++	2	-	10	-	12								-	1	2d	CH	10d	CH	12d	CH		A	++++	No follow-up

H—Hinton test
W—Wassermann test
HW—Hinton and Wassermann tests
*2 plus reaction.
†Born one month before term.

CH—Capillary Hinton test
K—Kahn test
Day—Days after birth

L.B.—Long bones
m—Months after birth
d—Days after birth

A—Acquired syphilis
C—Congenital syphilis
- —Negative
Col.—Colored

of life (Table II, No. 13), the titer of the capillary reaction rose sharply to a maximum by the twelfth day, and the regular Hinton test and x-ray films of the long bones were also positive. The delayed rise in the titer of the first blood in the series (Table II, No. 122) cannot be attributed entirely to failure to inactivate the serum in the first two specimens nor to inexperience in making the readings.

Since the capillary Davies-Hinton readings were made under the low power of the microscope, it was possible to detect minimal reactions not visible to the naked eye in the regular Hinton test. Therefore, it is not surprising to find the Hinton tests negative in most of the infants, even in those whose capillary tests were positive.

Six infants in the series were colored, including a pair of dizygotic twins (Table III, No. 23a and 23b) whose blood tests were at all times negative. The other four colored infants gave early positive reactions (Table II, No. 21, 59 and Table IV, 101, and 106).

The two cases of congenital syphilis (Table II, No. 13 and 35) which were detected are instructive. They may be briefly summarized as follows:

CASE 13.—A full-term infant, weighing 8 pounds and 4 ounces, appeared vigorous and free from stigmas of disease. The placenta was normal. The mother, aged 31, was a white, married, secundigravida who had had no treatment prior to this pregnancy. During the last two months of this pregnancy she received ten intravenous injections of an arsenical preparation. Her capillary "Davies-Hinton" test was 4 plus. The sibling was syphilitic. A capillary test of the infant obtained on the ninth day was 2 plus. Three days later it was 4 plus, and the regular Hinton test and x-ray films of the long bones were strongly positive. Hinton tests repeated when the infant was 17 days old, one month old, and at three months were all positive. This infant did well under specific treatment.

CASE 35.—The infant was born by cesarean section four weeks after the calculated time at which it was due. Its weight was 4 pounds and 8 ounces, length, 19 in. There were no stigmas of syphilis. The placenta was normal. The mother, aged 25, was a white, married, secundigravida whose first pregnancy six years previously had terminated in a miscarriage at three months. She had had no treatment, with the exception of two intravenous injections of an arsenical preparation during the last two weeks of this pregnancy. Her capillary test was 4 plus. The infant gained slowly while in the maternity hospital. X-ray films of the long bones taken on the second day were equivocal. The Hinton test on the fifth day was negative. The capillary blood test on the second day was 2 plus, on the tenth day 1 plus, and on the thirteenth day, negative. When the infant was 14 weeks old the mother took it to the clinic where she was being treated. No record was kept at this clinic of the general condition of the child at this time, but the Hinton and Wassermann reactions were positive then and again a week later. No x-ray pictures were taken. A diagnosis of congenital syphilis was made, and the infant was placed under treatment at once. This case illustrates the fact that the mere "washing out" of the early transmitted reaction from the mother does not preclude syphilis in the infant.

A rough correlation between the strength of the serologic reactions of the mothers and the incidence of positive reactions in the infants during

TABLE III

INFANTS BORN CONSECUTIVELY AT LEAST ONE YEAR BEFORE CONCLUSION OF THE STUDY

NEONATAL BLOOD TESTS NEGATIVE

SERIAL NUMBER	NEONATAL PERIOD								FOLLOW-UP PERIOD						MOTHER		REMARKS
	CAPILLARY HINTON TESTS NEGATIVE DAYS AFTER BIRTH				CORD HINTON	HINTON	DAY	WASSERMANN	DAY	X-RAY L.B.	DAY	AGE	TEST NEGATIVE	AGE	TEST NEGATIVE	AGE	TEST NEGATIVE	X-RAY NEGATIVE	SYPHILIS	CAPILLARY HINTON	
H	6	8	11			-	16			-									A	++++	Died after 1 mo., pneumonia
15	1	5	9		-					-	3	2m	H	9m	CH	13m	CH		A	++	Normal infant
14	1	4	12			-	0			-	1	17m	CH						A	-	Normal infant
23a	1	4	12							-	1	3m	CH	12m	CH				A		Normal girl } Twins†
23b	1	4	12							-	1	3m	CH	12m	CH				A		Normal boy } (Col.)
30	3	6								-		9m	CH					9m	A	++++	Developed scurvy
29	8									-	4	8m	CH	19m	CH				?C		Normal infant
44	12				-					-	11	8m	CH						A	-	Care of private physician
28	3	7				-	3			-	4	2m	CH	2m	H	12m	CH		A	+++	Normal infant
19	1	4				-	2			-	4	5m	HW	8m	HW	14m	HW		A	+++	Normal infant
51	4	6								-	1								A	++++	No follow-up
34	2	4			-					-	3								A	+	No follow-up
50	3	6	11									1m	CH	6m	CH	17m	CH		A	+++	Normal infant
B	2	4	19	24						-	2								C	++++	No follow-up*
F	5	7								-	4	2m	CH	9m	CH	15m	CH	2m	C	++++	Normal infant
38	1	5								-									?C	++	Care of private physician
A	3	5				-	5	-	5			2m	CH						A	+++	Follow-up incomplete
E	1	4				-	2	-	2	-	1	3m	CH	9m	HWK				A	-	Apparently normal
45	2	6	16			-	1	-	1	-	1	44d	CH	5m	CH	16m	CH	44d	A	++++	Normal infant
69	4	11				-	2	-	2	-	1	1m	CH	5m	CH	13m	CH		A	+	Normal infant
60	1	7			-	-	1	-	1	-	1	7m	CH						A	++	Nutritional anemia
64	1	3			-	-	1			-	1	2m	CH	3m	CH	16m	CH		A	+++	Normal infant

*Born two months before term. Capillary Hinton test negative, 12/28/37.
†Born one month before term.
See Table II for legend.

TABLE IV

INFANTS BORN CONSECUTIVELY FOUR TO TWELVE MONTHS BEFORE CONCLUSION OF THE STUDY

SERIAL NUMBER	NEONATAL PERIOD												FOLLOW-UP PERIOD				MOTHER		REMARKS
	CAPILLARY HINTON TESTS						CORD HINTON	HINTON		WASSERMANN		X-RAY L.B.		AGE	TEST NEGATIVE	AGE	TEST NEGATIVE	X-RAY NEGATIVE	SYPHILIS	CAPILLARY HINTON	
	RESULT	DAY	RESULT	DAY	RESULT	DAY		RESULT	DAY	RESULT	DAY	RESULT	DAY								
86	+++	2	+++	6				-	2	-	2	-	2						A	++++	Care of private physician
67	-	3	-	5				-	3	-	3	-	3	6m	H				A	+++	Apparently normal
70	-	1								-	2	-	0	6m	HWK				A		Apparently normal
85	-	1	-	6				-	1	-	1	-	1	7m	H			7m	A	+++	Apparently normal
97a	-	8	-	10								-		3m	H				?C		Twins, apparently normal
97b	-	8	-	10				-		-		-		3m	H				?C		
91	-	4	-	6				-	3	-	3	-	3						A	++++	Physical exam. neg. 11m
89	-	3	-	5				-	2	-	2	-	2	2m	HW				A	++++	Physical exam. neg. 4m
98	+++	2	-	5										4m	H			4m	A	++++	Apparently normal
100	++	6	++	9				Pos.	6	-	6	-	2	4m	H				A	++++	Apparently normal
102	+	8	+	11	++	22													A	++++	No follow-up in 6m
106	++	2	++	5				-	2	-	2	-	2						C	++++	No follow-up (Col.)
104	-	4	-	6				-	2	-	2	-	2	3m	H				A	++	Apparently normal
117	+++	3	+++	5	+	7	+	Pos.	1	Pos.	1	?	1	1m	CH	2m	CH		A	++++	HW positive on 7th day
109	-	2	-	5			20					-	2						A	+++	No follow-up in 4m
101	++	3	+	5	++	13	-	-	3			-	1						A	++++	No follow-up in 4 m (Col.)
							18														

*Born at home one month before term.
See Table II for legend.

the neonatal period was attempted (Table V). In both instances of congenital syphilis detected, the reaction in the serum of the mother was strongly positive (4 plus).

TABLE V

COMPARISON OF THE STRENGTH OF THE REACTION IN THE MOTHER'S BLOOD WITH THE NEONATAL REACTION IN THE INFANT (CAPILLARY "DAVIES-HINTON" TEST)

		MOTHER		
		4 PLUS	3 PLUS TO 1 PLUS	NEGATIVE
Infant	Positive	21	2	0
	Negative	8	15	3
	Total	29	17	3

From the foregoing study of the serologic reactions of a series of infants whose mothers have had syphilis, certain observations appear to be justified:

1. The stronger the positive reaction in the mother the greater the likelihood of a positive reaction in the newborn infant (Table V).

2. Although in most instances the transmitted positive reaction in the blood of the infants diminished or disappeared entirely within two weeks after birth, in one case (Table II, No. 122) it was detectable by the sensitive method employed for at least three months after birth and in another case (Table II, No. 21) for at least forty days. Both infants were kept under observation for more than one year and at the end of this time were discharged as nonsyphilitic.

3. In one case (Table II, No. 35) the transmitted positive reaction disappeared before the development by the syphilitic infant of specific reagins demonstrable in the blood.

4. Eleven infants whose neonatal blood tests were positive were followed clinically and serologically for six months or more. Two of these were recognized as having congenital syphilis. Nine were symptom-free at the end of one year.

5. Of the nineteen infants followed for at least six months, whose neonatal blood tests were consistently negative, none developed evidence of congenital syphilis. Twelve of these nineteen were followed for one year or more.

6. Employing a sensitive serologic test for syphilis, almost one-half (25 out of 56) of the infants in this series had positive neonatal blood tests, and yet congenital syphilis was detected in only two.

7. Seven infants born of mothers with congenital syphilis gave early positive serologic reactions. One died at 3 months of age, apparently nonsyphilitic; one was negative at 1 month of age and was not seen again; and one was not examined after leaving the maternity hospital. Four of the seven infants were kept under observation for over one year and at the last examination were clinically and serologically negative.

CONCLUSIONS

1. The results support Fildes' law that the neonatal positive reaction may simply reflect the existence of a positive reaction in the mother and is not of itself* a criterion of syphilitic infection of the infant nor an indication for treatment.

2. Infants born of syphilitic mothers whose neonatal blood tests are positive are more likely to develop evidence of congenital syphilis than those infants whose early blood tests are negative, and, therefore, the seropositive infants should be kept under particularly close observation.

3. The diminution in strength or the disappearance of the early positive reaction does not necessarily mean freedom from infection.

4. The age at which one should cease to discount the early positive reaction and at which a strongly and consistently positive reaction points to congenital syphilis is probably between 3 and 4 months after full-term birth.

5. The development of two or more strongly positive blood tests at any time after a negative test points strongly to actual infection and is an indication for energetic search for confirmatory evidence.

6. Unless a diagnosis of congenital syphilis has already been established, every infant born of a syphilitic mother should have periodic examinations, including efficient blood tests, for at least six months and preferably for one year.

SUMMARY

A series of fifty-six infants born of syphilitic mothers were studied by means of physical examinations and repeated "Davies-Hinton" micro-flocculation tests on serum obtained by skin puncture, together with x-ray films of the long bones and supplementary tests on blood obtained by venepuncture. An estimate of the strength of the reaction in the infant and in the mother was made. Twenty infants, including two in whom congenital syphilis was detected, were kept under observation for at least one year. Syphilis was recognized in one of these infants by serologic tests and x-ray films of the long bones before the development of outward evidence of the disease; in the other infant no physical signs were recorded. The length of time the transmitted positive reaction persists in the newborn infant and the apparent significance of a rising and a falling titer were noted. The study demonstrates the importance of a rigid follow-up system and lends support to the public health measures already being inaugurated.

Mrs. M. H. Walter and Mrs. R. S. Field were of great assistance in securing the return of the infants for follow-up examinations. Mrs. Walter helped prepare the material.

*A possible exception is a titer in excess of that of the mother, which may indicate syphilis in the infant.

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DIPHTHERITIC POLYNEURITIS

A Report of Nine Cases

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DURING 1937 twenty-five children with diphtheria were admitted to Duke Hospital, nine of whom had polyneuritis due to their infection. A total of ninety-two cases of diphtheria had been admitted from 1930 to 1937, yet only five of these patients had postdiphtheritic paralysis.

It is generally stated that some form of neuritis develops in from 10 to 20 per cent of all cases of diphtheria. Paralysis may occur in treated cases of diphtheria as well as in those in which the nature of the throat infection has not been recognized. In treated cases, the earlier the antitoxin is given the less likelihood there is of paralysis developing. In Rolleston's large series,[1] only 3.6 per cent of the patients receiving antitoxin on the first day subsequently developed paralysis, whereas when antitoxin was not given until the third day, 21.4 per cent developed paralysis, and when specific therapy was delayed until the sixth day, 27.1 per cent developed some form of neuritis.

It seems to be well established that paralysis following diphtheria is due to the production of a neurotropic toxin which is absorbed by the blood stream and carried throughout the body. Walshe,[2] analyzing the mechanism of diphtheritic paralysis as a result of a study of wounds infected by the diphtheria bacillus, divided the neuritis into three groups: (1) the local, or regional, (2) the specific, and (3) the general. The local paralysis is well demonstrated by the involvement of the palate due to the direct action of the toxin. The paralysis of the ciliary muscle is called specific because it is peculiar to diphtheria and may occur even in the absence of general paralysis. Finally, generalized paralysis or polyneuritis is due to the presence of toxin in the blood stream. The investigations of Abel[3] on the pathways by which tetanus toxin reaches the nervous system would seem to apply with equal force to the diphtheritic toxin.

The sequence of the paralysis is quite uniform, the local, specific, and generalized type of paralysis following in the order named. The paralysis of the palate is usually the first and may be the only involvement. This is generally seen at the end of the second week of the illness, but

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may appear sooner. The later it appears, the less likely is the paralysis to be widespread. At about the same time, paralysis of the muscles of the pharynx and larynx may be noted. The ocular palsies appear about the third week, involving mainly the muscles of accommodation and less frequently the extraocular muscles. General paralysis rarely develops before the fifth week. Palsies of the lip or of the facial muscles and of the vesical and rectal sphincters may also occur at this period. These may be involved alone or in combination. Respiratory paralysis is seen late in the course of the disease and only in severe cases. It is due mainly to involvement of the phrenic nerves, although paralysis of the accessory muscles of respiration may also be a complicating factor. The deep reflexes, especially the knee jerks, are frequently abolished, even when the process is mild, but the superficial reflexes are retained, unless the neuritis is widespread.

Our patients were all seen late, and local as well as generalized paralysis had developed. Six of the nine children had such mild attacks of diphtheria that they were not recognized as such and therefore not treated. The three treated children received only 10,000 units of diphtheria antitoxin late in the course of the disease, one as late as the sixteenth day.

Of the nine children, three were referred to the hospital with a diagnosis of acute anterior poliomyelitis, two as having brain abscesses, and one with Bell's palsy; the remaining three were correctly diagnosed. Two of the nine children died with myocardial failure. Seven recovered in periods ranging from one to four months.

One child with a preceding history of membranous pharyngitis had only a facial paralysis and absent knee jerks; the child was referred to the clinic with a diagnosis of Bell's palsy. On investigating the ten cases of Bell's palsy on file in the record room it was interesting to note that all of them occurred during the months of November, December, and January—the diphtheria months. Perhaps on closer observation some of these palsies may have had a diphtheritic origin.

Seven of the nine patients still had positive culture for the Klebs-Löffler bacillus when admitted; unfortunately, virulence tests were not done. The Schick tests were uniformly negative. The spinal fluid findings on four patients were entirely normal. Six patients were studied electrocardiographically, but only one had any evidence of myocardial damage. This finding does not correspond with the results obtained by Burkhardt et al.[4] Sixty-five per cent of their large series of patients presenting electrocardiographic changes had peripheral nerve palsies of various degrees. The one child who had electrocardiographic changes died on the sixth hospital day. The only other fatality occurred in a boy with a generalized paralysis and physical signs of myocardial damage, who was moribund when admitted to the hospital and died soon afterwards.

As soon as the diagnosis was clarified, six of the patients received 10,000 to 20,000 units of diphtheria antitoxin without apparent benefit. The daily intravenous injection of 5 or 10 per cent glucose did not appear to influence the course of the disease. The weakened extremities were treated with heat, massage, and passive motion. Immobilization was necessary in only three cases. In the main, treatment consisted of complete bed rest, sedation, and gavage feedings if the pharyngeal paralysis was sufficient to interfere with swallowing. The Drinker respirator was lifesaving to the child with the complete respiratory paralysis, and because of the unusual features of this case it is reported in detail.

CASE REPORT

History.—B. M., a five-year-old white girl entered Duke Hospital on Feb. 26, 1937, because of weakness of the extremities of five weeks' duration. During the latter part of November, 1936, she developed sore throat, and a diagnosis of tonsillar diphtheria was made. She was given 10,000 units of diphtheria antitoxin and made what was apparently a complete recovery. On Jan. 15, 1937, she complained of being tired, lost her appetite, and became constipated. Two weeks later the parents noticed a definite weakness of the lower extremities which progressed to involve the upper extremities also. The past history was interesting in that the patient had been immunized one year previously against diphtheria.

Physical Examination revealed a well-developed, poorly-nourished 5-year-old girl who was lying quietly in bed. She was able to move only her left hand. Respirations were normal. Her voice was soft, but she spoke clearly and distinctly. The cervical and inguinal nodes were moderately enlarged. The pupils were equal and reacted well to light and accommodation. The tonsils were enlarged and hyperemic, and there was a mucopurulent discharge in the posterior pharynx. The heart and lungs were clinically negative. The upper extremities were extremely flaccid. She could extend her arms but could not flex them. There was limitation of both abduction and adduction, and she was able only slightly to flex and extend her fingers. Extension and flexion of the lower extremities were markedly limited. The periosteal radial reflexes were equal and active. No other reflexes could be obtained. The cranial nerves were intact except for the sixth (limitation of lateral deviation).

Laboratory Tests.—The blood count showed the following: Hb. 15 gm. (97 per cent, Sahli); red blood cells 4,940,000; white blood cells 6,100, with normal differential. Throat culture was negative for the Klebs-Löffler bacillus. Urinalysis and stool examination were both negative. Spinal fluid revealed normal cytology and dynamics. Glucose tolerance test was normal. Wassermann, Schick, and Tuberculin (0.1 mg. with old tuberculin) tests were negative.

Course.—The patient received 20,000 units of diphtheria antitoxin soon after admission, and 100 c.c. of 10 per cent glucose were given intravenously daily for the first nine days. There was no improvement following the above therapy. Two weeks after entering the hospital it was noted that the patient had developed a thoracic type of breathing. Fluoroscopic examination of the chest showed the lungs to be clear, but the diaphragms, which were smooth in outline, failed to move.

During the next eight days the involvement became more pronounced until on March 20, 1937, the respiratory distress became alarming and the patient was removed to the Johns Hopkins Hospital where she could be placed in a respirator. She remained in the respirator for two months, by which time the diaphragmatic paralysis

TABLE I

SUMMARY OF NINE CASES OF DIPHTHERITIC PARALYSIS

AGE	SEX	RACE	PRECEDING RESPIRATORY INFECTION	ANTITOXIN		THROAT CULTURE	SCHICK TEST	SPINAL FLUID	EKG	PARALYSIS AND COMMENT
				HOME	HOSPITAL					
6	M	W	Yes	0	10,000	Pos.	0	Neg.	Normal	Generalized muscular weakness, more marked on left. Apparent recovery by the end of three months.
1	F	W	No	0	10,000	Pos.	0	Neg.	--	Flaccid paralysis of the left leg. Improved over a period of two months.
7	M	W	Yes	Yes; 16th day; am't unknown	10,000	Pos.	0	--	Myocardial damage	5th, 7th, 9th, 11th, and 12th cranial nerve. Marked generalized weakness of muscles. Died on 6th hospital day.
10	M	W	Yes	0	0	Pos.	0	--	--	Bell's palsy with absent knee jerks. Recovery in three months.
4	M	W	Yes	0	10,000	Pos.	0	Neg.	Normal	Facial, laryngeal paralysis and generalized weakness, more marked on left, absent deep reflexes. Was considered to have brain abscess. Marked improvement in one month.
2	M	W	Yes	0	0	Pos.	--	--	--	Laryngeal, palatal, and generalized flaccid paralysis. Died soon after admission to the hospital.
3	M	W	Yes	0	0	Neg.	--	--	Normal	Palatal, facial, and generalized flaccid paralysis. Discharged day after admission against advice.
5	F	W	Yes	Yes; am't unknown	20,000	Neg.	0	Neg.	Normal	Facial, palatal, and diaphragmatic, with ascending paralysis of Landry type. Four months in respirator. Recovered.
4	M	W	Yes	Yes; 4 days after ill.	20,000	Pos.	0	--	Normal	Palatal, generalized flaccid paralysis which showed marked improvement in one month.

had cleared entirely. At the same time there was marked improvement of the paralysis of the extremities, and only a weakness of the dorsiflexors of the feet remained. When last heard from the patient had made a complete recovery.

CONCLUSION

1. Nine cases of diphtheritic paralysis occurring during the year 1937 are recorded.

2. The etiology, types, course, and treatment of diphtheritic paralysis are discussed.

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THE TREATMENT OF MENINGOCOCCUS MENINGITIS

Intraspinal Use of Antimeningococcus Serum at Bellevue Hospital, 1928 to 1936

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THE final test of any therapeutic procedure or substance is the benefit obtained by the patient, either in the saving of his life or in the rapidity of his convalescence from a serious disease. It is well known that meningococcus meningitis is just such a serious disease with a high case fatality rate and is attended by serious sequelae for those who survive. In the evaluation of its treatment several criteria are available, chief among which is the case fatality rate. Any form of treatment which can bring about a marked reduction in the rate in a large series of cases must be acknowledged as extremely desirable.

The purpose of this paper, dealing with the experience in the intraspinal use of antimeningococcus serum at Bellevue Hospital, is to demonstrate the value of such use as reflected in the course of the case fatality rate from 1928 through 1936. The results obtained will be seen to confirm the idea that the proper use of a potent antimeningococcus serum intraspinally is an adequate and valuable method of treatment. No attempt will be made to elucidate the nature of meningococcus meningitis; whether it is primarily a systemic disease with local manifestations in the nervous system or a local disease of the nervous system with systemic manifestations will not be discussed. However, since the pathologic changes occurring in acute meningococcus meningitis involve mainly the nervous system, and since the sequelae are most frequently manifestations of these changes (deafness, blindness, cerebral damage), treatment should be aimed at preventing their occurrence. This report is concerned with the treatment by intraspinal administration of a potent antimeningococcus serum.

Scope.—This study deals with the records of 191 patients from infancy to 12 years of age, admitted with meningococcus meningitis to the Children's Medical Service of Bellevue Hospital from 1928 through 1936. The data obtained from an analysis of the bedside records are presented in Tables I to V. Practically all the patients were seen or attended by one of the observers who contributed the summaries.

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This paper is based on summaries compiled by resident physicians on the Children's Medical Service: Dr. Julian Price, for the years 1912 to 1928, Dr. Norman Coward, 1928 to 1932, Dr. Dorothy Geib 1932 to 1935, and the writer, 1935 to 1936. Credit and thanks are due them for the excellency of their abstracts.

METHOD OF TREATMENT

During the years 1928 to 1932 the majority of the patients received serum intraspinally once every twenty-four hours, while from 1932 to 1936 serum was given intraspinally every twelve hours for the first few days. On admission to the hospital a patient suspected of having meningitis underwent lumbar puncture. If the spinal fluid was at all cloudy, as much of it as possible (usually 20 to 30 c.c.) was withdrawn, and 20 c.c. of antimeningococcus serum (prepared by the New York City or New York State Health Department) was allowed to run in by gravity. A specimen of the spinal fluid was examined for: cell count, sugar, protein, and organisms, by smear and culture.

The administration of serum intraspinally was continued at daily or twelve hour intervals until definite improvement was noted. The criteria for discontinuing serum therapy were as follows: (1) decrease of spinal fluid pleocytosis to about 500 cells or less; (2) normal or rapidly falling blood leucocytosis; (3) rising spinal fluid sugar; and (4) persistent negative spinal fluid culture.

From the practical standpoint it is well to emphasize the value of the first two laboratory factors in arriving at a decision. Both can be rapidly determined at the bedside, and it has been our experience that their answer is usually confirmed by the subsequent report of a negative culture and by the recovery of the patient. In our series of patients, if the above criteria had not been attained after four or five days of treatment, a change in the type of serum (from City to State or vice versa) was made, often with a happy outcome.

RESULTS

In the whole series of 191 patients on whom we are reporting there were forty-eight deaths, a *crude* case fatality rate of 25 per cent. This includes one patient who died of a secondary streptococcus meningitis and eighteen patients who received either no treatment at all (diagnosis post mortem) or who died within twelve hours of the initiation of therapy. In the group of 191 patients there were also some who were admitted with residual signs of a previously treated meningitis and who required no active specific therapy.

In all then, there were 169 patients treated, of whom twenty-nine died, a case fatality rate for the whole nine year period of 17 per cent. Before going on to a more detailed consideration of this rate, a brief summary of the more salient clinical features will be given.

Age Distribution.—A study of the age distribution (Table I) of the 191 patients shows that there were forty-one (22 per cent) less than 2 years old, seventy-three (38 per cent) more than 2 and under 7 years old, and seventy-seven (40 per cent) more than 7 and less than 12 years of age. In the years 1928 to 1929 there were relatively

more infants, 25 per cent under 2 years of age, while in 1935 to 1936 about 16 per cent of the patients were in this age group. This change in age distribution from 1928 to 1936 has a definite bearing on a change in case fatality to be discussed later. That the disease tends to attack a somewhat older age group in more recent years has also been noted in New York City as a whole.

TABLE I

MENINGOCOCCUS MENINGITIS AT BELLEVUE HOSPITAL

		1928	1929	1930	1931	1932	1933	1934	1935	1936	Total
Number of cases		77	32	14	11	4	5	1	29	18	191
Number of cases treated		67	27	11	10	3	4	1	28	18	169
Males		29	17	7	7	1	1	1	21	9	93
Females		22	15	7	4	3	4	0	8	9	72
Less than 2 years old	cases	18	8	4	1	0	2	0	4	4	41
	deaths	15	2	2	1	0	1	0	1	0	22
2 years old and less than 7	cases	25	11	8	6	3	2	0	11	7	73
	deaths	6	3	1	1	2	0	0	1	2	16
7 years old and less than 12	cases	34	13	2	4	1	1	1	14	7	77
	deaths	7	2	0	0	0	0	1	0	0	10
Deaths, all cases		28	7	3	2	2	1	1	2	2	48
Deaths, in treated cases		18	4	1	1	1	0	1	1	2	29

Sex Distribution.—In the whole series there were 165 records on which sex was indicated, and from Table I we see that ninety-three (57 per cent) were males, and seventy-two (43 per cent) were females. This is in line with other studies showing a preponderance of males among the victims of the disease.

DURATION OF DISEASE ON ADMISSION AND INITIAL SYMPTOMS

From Table II we see that 133 (70 per cent) of the patients were admitted before the fourth day of illness. In the earlier years (1928 and 1929) this percentage is somewhat lower and in the later years (1935 and 1936) somewhat higher.

TABLE II

DURATION OF DISEASE ON ADMISSION

		1928	1929	1930	1931	1932	1933	1934	1935	1936	Total
Under 1 day	cases	30	11	4	4	1	2	0	14	6	72
	deaths	6	1	1	1	0	1	0	1	0	11
1 to 3 days	cases	21	8	5	5	2	1	1	9	9	61
	deaths	13	4	1	1	1	0	1	0	0	21
Over 3 days	cases	26	13	5	2	1	2	0	6	3	58
	deaths	9	2	1	0	1	0	0	1	2	16

The usual clinical features were noted: A rather abrupt onset with headache, vomiting, drowsiness, and nuchal stiffness were the outstanding signs and symptoms. A rash, usually petechial, occasionally purpuric, infrequently macular or morbilliform, was noted in ninety-

seven or about 50 per cent of the patients. Among these ninety-seven patients there were twenty-five deaths. Among ninety-four patients without a rash there were twenty-three deaths. This confirmed our clinical impression that the presence of a rash is no indication of the severity of the disease. As a matter of fact, there was no definite sign, symptom, or group of signs or symptoms which helped in determining the prognosis when the patient was first seen. Some patients who looked very sick on admission recovered uneventfully, while others who seemed only moderately ill died.

TABLE III

		1928	1929	1930	1931	1932	1933	1934	1935	1936	Total
Rash on admission	cases	37	12	5	5	3	4	0	20	11	97
	deaths	12	4	1	1	2	1	0	2	2	25
Positive spinal fluid, culture or smear		60	24	8	5	3	5	1	24	16	146
Complications	eye	8	7	1	0	0	0	0	1	2	19
	ears	13	4	4	2	0	1	0	4	4	32
	joints	3	4	1	0	1	0	0	4	3	16

Complications.—From 35 to 40 per cent of the patients developed one or more complications. The more frequent complications encountered were arthritis, otitis media and mastoiditis, nerve deafness, ophthalmitis, and blindness (Table III).

Positive cultures.—The meningococcus was found in the spinal fluid by smear or culture in 146 (74 per cent) of the 191 cases studied. The remaining 26 per cent, with negative or doubtful smear or culture, showed either unequivocal clinical features or a rapid response to specific treatment, so that the diagnosis was not at all doubtful.

TABLE IV

TREATMENT

		1928	1929	1930	1931	1932	1933	1934	1935	1936	Total
Intraspinal administration	every 24 hr.	63	27	10	10	3	2	0	0	1	116
	every 12 hr.	4	0	1	0	0	2	1	28	17	53
One treatment or none		10	5	3	1	1	1	0	1	0	22
Intravenous serum	cases	10	3	2	1	0	2	1	21	8	48
	deaths	3	1	0	0	0	2	1	1	2	10
Average amount serum per patient (c.c.)		157	150	180	125	–	–	–	165	165	125-180
Serum sickness, cases		26	16	8	6	2	3	0	15	12	88

TREATMENT

Average Amount of Serum Used.—In 1928 and 1929 about 155 c.c. of serum were used per patient, and in 1935 and 1936 this average was 165 c.c.—a difference that is not remarkable. It shows that not much more serum needs to be used for each patient when treated twice daily than when treated only once.

Serum disease.—Serum disease as evidenced by an urticarial eruption, sometimes with fever and joint symptoms, was noted in about 48 per cent of the cases. No immediate anaphylactic severe or fatal serum reaction was noted. The serum disease usually occurred from four to seven days after initiation of treatment. A point to be noted here is the occasional difficulty of differentiating serum arthralgia from a complicating arthritis due to the meningococcus. The latter usually can be definitely established by aspiration.

Intravenous serum.—Of forty-eight patients between 1928 and 1936 who received serum by the intravenous as well as by the intraspinal route (usually 20 to 30 c.c. intravenously) ten (21 per cent) died. Among those who did not receive intravenous serum we find 143 patients with thirty-eight deaths, a case fatality of 26 per cent.

Case fatality.—During 1928 and 1929 and again during 1935 and 1936 the disease was prevalent in New York City in epidemic proportions. As a result these years give us an adequate number of cases for comparison of case fatality. From Table I we can abstract the following:

TABLE V

	1928-1929	1935-1936
Number of cases treated	94	46
Number of deaths	22	3
Case fatality	23%	7%

We believe that the case fatality for 1935 and 1936 of forty-six patients with but three deaths is ample confirmation of our faith in the orthodox method of therapy. At Post-Graduate Hospital Dr. Charles J. Leslie has noted correspondingly good results (personal communication).

TABLE VI

		1928*	1929-1932	1933-1937
Post-Graduate Hospital	cases	44	49	23
	deaths	14	12	3
Case fatality		32%	24%	13%
Bellevue Hospital	cases	67	51	51
	deaths	18	7	4
Case fatality		27%	14%	8%

*De Sanctis: Am. J. Dis. Child. 38: 730, 1929.

There was only one essential difference in the method of treatment at Bellevue Hospital from that at the Post-Graduate Hospital, namely, in the frequency of dosage. At Bellevue, in 1933 to 1936, the serum was given every twelve hours, while at the Post-Graduate Hospital the twenty-four-hour interval was employed. The sera used were the same in both hospitals, the hospitals drew patients from the same type of population, and the characteristics of the disease were the same in the two places.

Before taking the remarkable reduction in case fatality at Bellevue from 23 per cent to 7 per cent (Table V) at its face value, we should remember the influence of a greater proportion of infants in 1928 and 1929. Since the fatality rate in that age group was 68 per cent in those years, an unduly high figure, it is only fair to compare the older age groups without regarding the fatality in infants.

TABLE VII

CASE FATALITY IN AGE GROUP OF PATIENTS MORE THAN 2 YEARS OLD

	1928-1929	1935-1936
Cases	83	39
Deaths	18	3
Case Fatality	22%	8%

The difference between the two periods becomes slightly less when regarded from this standpoint.

A second factor to be noted in comparing 1928 and 1929 with 1935 and 1936 is the slightly longer duration of illness before diagnosis and treatment in 1928 and 1929. In those years 74 per cent of the patients received treatment before the fourth day of illness, while in 1935 and 1936 82 per cent of the patients were treated before the fourth day.

Both of these considerations modify the reduction in case fatality from 1928 and 1929 to 1935 and 1936 in the sense that it is somewhat smaller than would at first appear.

TABLE VIII

HOSPITAL STAY

	1928	1929	1930	1931	1932	1933	1934	1935	1936	Total
Less than 1 week, including deaths	21	8	2	1	1	1	0	3	1	38
1 week and less than 2	9	3	2	3	1	1	1	12	6	38
2 weeks and less than 4	28	13	7	6	2	2	0	9	9	76
Over 4 weeks	19	8	3	1	0	1	0	5	2	39

HOSPITAL STAY

During 1928 and 1929, of eighty patients who survived one week, sixty-eight (85 per cent) stayed longer than two weeks in the hospital. In 1935 and 1936, of forty-three patients who survived one week, only twenty-five or less than 60 per cent stayed longer than two weeks. In other words, in 1928 and 1929 less than two out of ten survivors left before the second week was over, while in 1935 and 1936 more than four out of ten left the hospital before their fourteenth hospital day.

DISCUSSION

In seeking a cause for the marked reduction in the case fatality rate and in the period of hospitalization from 1928 through 1936 in our series of patients, we felt at first that the twelve-hour interval of serum

administration used in the latter years (1935 and 1936) was largely responsible. However, two other possibilities had to be considered, namely, a change in the virulence of the organism and an increase in the potency of the serum used.

For New York City as a whole the following figures were obtained from the New York City Health Department.

TABLE IX

MENINGOCOCCUS MENINGITIS, NEW YORK CITY

	1928	1929	1935	1936
Cases	1102	1000	529	538
Deaths	540	486	244	226
Case fatality	49%	49%	46%	42%

It seems fair to conclude that the organisms responsible for the 1935 and 1936 outbreak were quite as virulent as those in 1928 and 1929.

Since the reduction at Bellevue Hospital in the case fatality rate was paralleled, albeit at a somewhat higher level, by one at another hospital using the same type of sera, it is fair to conclude that a part of the reduction in case fatality must be ascribed to an increase in the potency of the sera used. Nevertheless, we still feel that the twelve-hour interval in dosage contributed in part to the reduction. This conclusion is based on a fatality rate at Bellevue Hospital about one-third lower than that at the Post-Graduate Hospital during a similar period.

SUMMARY

Our belief is that the intraspinal administration of a potent antimeningococcus serum every twelve hours for the first few days gives better results than when given at longer intervals. The case fatality rate is lower, the hospital stay is shortened, and the total amount of serum used is not much, if any, greater. Further reduction in case fatality is to be sought in earlier diagnosis and in the use of as potent a serum as can be manufactured. The reasons outlined in the beginning of this paper for intraspinal administration of antimeningococcus serum, rather than the intravenous use of antitoxin alone, we believe to be supported by our results.

GAUCHER'S DISEASE IN EARLY INFANCY

Review of Literature and Report of Case With Neurological Symptoms

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IN 1924 Reuben[39] called attention to the relative frequency of Gaucher's disease occurring in childhood, and in addition pointed out the relationship existing between age of onset and duration of the disease. Three years later Oberling and Woringer[33] reported on the outstanding difference between the manifestations of the disease in infancy, on the one hand, and in adults and older children, on the other. They observed four cases in infants occurring in the same family and all of which, in addition to the usual splenohepatomegaly, showed a remarkable neurological syndrome. Each of these four patients had a retraction of the head with rigidity of the neck, opisthotonus, spastic extremities, laryngeal spasms, dysphagia, trismus, strabismus, and a tendency to maintain the arms in certain positions for long periods of time. Three of these patients gave evidence of progressive loss of sensation and complete lack of interest in the environment. At autopsy of these cases pronounced changes were observed in the cerebral cortex, but the remaining portions of the brain were spared.

Prior to the appearance of the above mentioned case reports, Rusca,[41] Kraus,[23] Kohn,[22] Pick[34] and Nauwerck,[32] and Reber[36] had published cases in which this neurological syndrome existed to a greater or lesser extent, but upon which these observers placed no particular stress. Meyer,[29] collecting fourteen of such cases from the literature and adding one of his own, gave an elaborate description of the neurological picture which he considered to be a pseudobulbar syndrome. In this country, Hoffman and Makler[18] were the first to report a case of Gaucher's disease with neurological symptoms, but in some respects their case is exceptional. Winter[47] presented a fairly typical case of the disease, but he erroneously reported it as Niemann-Pick's disease. Rowland[40] gave a complete review of the subject and introduced the term "acute Gaucher's disease," by which term he excluded practically all except the neurological cases.

The present authors have collected from the literature a total of seventeen cases of Gaucher's disease occurring in infancy, and the predominating neurological symptoms of these cases are summarized in Table I. In addition to these, there are in the literature ten reported cases in which the onset of the disease had taken place during the first year of life but in which neurological manifestations were totally absent. With one exception these latter infants were past six months of age

TABLE I

CASES OF GAUCHER'S DISEASE WITH NEUROLOGICAL MANIFESTATIONS

AUTHOR (YEAR)	SEX	AGE OF ONSET	FIRST SEEN	AGE AT DEATH	FAMILY HISTORY	NEUROLOGICAL MANIFESTATIONS	SPLEEN	LIVER	HEMOGRAM AND BLOOD CHEMISTRY	OTHER FINDINGS
Rusca (1921)	M	6 mo.	11 mo.	12 mo.	–	Rigid neck; strabismus, hypotonia.	237 gm.	390 gm.	R.B.C. 3.10; Hb. 40% W.B.C. 10,000	Slight discoloration of skin; involvement of tracheobronchial, cervical, and inguinal nodes; femur and rib marrow affected.
Kraus 1921	F	6 mo.	7 mo.	12 mo.	–	Hypertonicity; convergent strabismus; mental retardation.	70 gm. To level of umbilicus	240 gm.		Premature; slight discoloration of the skin; mesenteric and peribronchial nodes affected.
Kohn (1921)	F	Since birth	9 mo.	9 mo.	–	Some neurological involvement.	310 gm.	–		
Pick-Nauwerck (1922)	M	–	8 mo.	8 mo.	–	Not mentioned.	80 gm.	Not enlarged		
Reber 1–(1924)	M	6 mo.	6 mo.	8 mo.	+	Neck rigidity; dysphagia; laryngeal spasm; hypertonicity; increased deep reflexes.	Markedly enlarged	Markedly enlarged		Diagnosis at autopsy; fever present.
Reber 2–(1924)	F	5 mo.	6 mo.	7 mo.	+	Neck rigidity; hypertonicity; increased deep reflexes; spasmodic cough unassociated with lung lesions.	Down to iliac crest	2 fingers below costal margin	R.B.C. 4.00; Hb. 62% W.B.C. 11,800	Pigmentation in spots over dorsum of fingers; febrile attacks.
Oberling-Woringer 1–(1927)	M	5 mo.	5 mo.	8 mo.	+	Opisthotonus; convergent strabismus; choking spells with convulsions; very marked apathy and sensory loss.				Abdomen prominent and indurated.

TABLE I—CONT'D

AUTHOR (YEAR)	SEX	AGE OF ONSET	FIRST SEEN	AGE AT DEATH	FAMILY HISTORY	NEUROLOGICAL MANIFESTATIONS	SPLEEN	LIVER	HEMOGRAM AND BLOOD CHEMISTRY	OTHER FINDINGS
Oberling-Woringer 2–(1927)	F	6 wk.	5 mo.	11 mo.	+	Strabismus; catatonia; apathy; dysphagia; laryngeal spasm; opisthotonus; marked hypertonicity; increased deep reflexes; trismus; mental and physical retardation.	To pelvis	To right iliac crest	R.B.C. 5.19	Slight cervical lymphadenopathy; sudden death; symptoms progressed in spite of antisyphilitic treatment
Oberling-Woringer 3–(1927)	F	6 wk.	5 mo.	11.5 mo.	+	Opisthotonus; laryngeal spasm; very marked hypertonicity; apathy; poverty of movements; trismus; convergent strabismus; increased deep reflexes; clonic convulsions; dysphagia; sensory loss.	1 finger above pubis	2½ fingers below costal margin	R.B.C. 4.40; Hb. 54%; W.B.C. 6,300; platelets 66,500.	Apparent death from asphyxia on several occasions; pallor.
Oberling-Woringer 4–(1927)	M	4 wk.	1 mo.	1 mo.	+	Apathy and poverty of movement.	Slightly enlarged	Enlarged	R.B.C. 4.35; Hb. 75%; W.B.C. 5,700	Marked pallor
Dienst-Hamperl (1927)	F	2 mo.	3 mo.	5 mo.	+	Opisthotonus; strabismus; hypertonicity; laryngeal spasms.	2 fingers below costal margin	3 fingers below costal margin	Hb. 50 %; increased urobilin in urine; cholesterol, 240.	Yellow discoloration of skin; diaphragmatic breathing; reported as Niemann-Pick's disease by Dienst; autopsy by Hamperl demonstrated Gaucher cells; sister of Stransky's patient.
Hoffman-Makler (1929)	M	–	17 mo.	17.5 mo.	–	Neck rigidity; hypertonic extremities; increased reflexes.	To umbilicus	Below umbilicus	R.B.C. 4.00; Hb. 70%; W.B.C. 26,000; cholesterol, 80; total fat 349.	Generalized lymphadenopathy; diagnosis by biopsy of lymph node.

TABLE I—CONT'D

Stransky (1930)	M	4 mo.	5 mo.	6 mo.	+	Opisthotonus; hypertonicity; stridulous breathing; stupor.	To iliac crest	3 fingers below costal margin	Phosphatides 9.5; R.B.C. 2.40; Hb. 58%; cholesterol, 135.	Continuous fever; brownish yellow tint of face.
Monerief (1930)	M	10 wk.	10 wk.	4 mo.	–	Opisthotonus; hyperactive deep reflexes.	2 fingers below costal margin	Not enlarged		Examination of liver showed Gaucher cells despite absence of enlargement.
Meyer (1932)	F	6 mo.	7 mo.	9.5 mo.	–	Dysphagia; opisthotonus; convergent strabismus; laryngeal spasms; catatonia; poverty and slowness of movement; hemiplegia.	2 fingers below costal margin	2 fingers below costal margin	R.B.C. 3.00; Hb. 62%; W.B.C. 9,400; platelets, 80,000.	Febrile attacks; clinical diagnosis confirmed by splenic puncture.
Winter (1932)	F	3 mo.	4 mo.	8 mo.	+	Unable to look to one side (left); unable to take feedings; opisthotonus; hypertonicity.	3 cm. below costal margin	2 cm. below costal margin	R.B.C. 4.00; Hb. 80%; W.B.C. 7,600; platelets 80,000	Splenic puncture showed Gaucher cells, but case reported as Niemann-Pick's disease.
Meyer (1934)	F	4 mo.	4 mo.	7.5 mo.	+	Opisthotonus; rigidity of neck; poverty and slowness of movement; strabismus; catatonia; laryngeal spasms.	2 cm. above iliac crest	3 cm. below costal margin		Fifth member of family studied by Woringer and Oberling.
Authors (observed in 1937)	F	1 wk.	2.5 mo.	4.5 mo.	–	Opisthotonus; neck rigidity; hypertonicity; strabismus; dysphagia; laryngeal spasms; catatonia of extremities.	To iliac crest	3 cm. below costal margin	R.B.C. 4.85; Hb. 65%; W.B.C. 11,600; cholesterol, 129.	Cervical lymphadenopathy; discoloration of skin; febrile attacks; clinical diagnosis confirmed by finding Gaucher cells in sternal marrow material.

when the first symptoms appeared, in contrast to the group displaying neurological symptoms and wherein the onset occurred in the first half year of life. In both groups, however, the course was rapid with fatal termination. The salient features of the cases occurring under six months are summarized in Table II. The nature of the case here reported establishes it as belonging to the group of Gaucher's disease indicated in Table I.

REPORT OF CASE

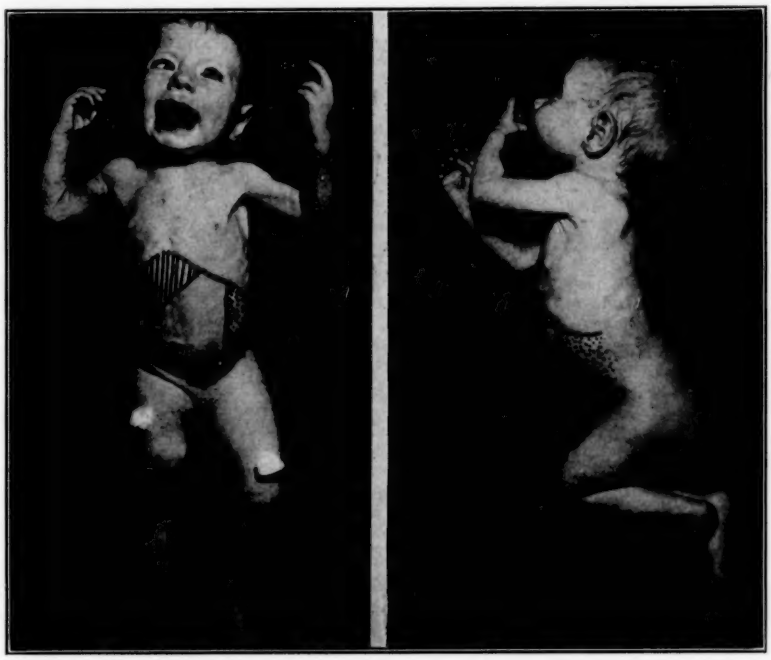
C. R., a white female infant, was born at term of a low forceps delivery at the Chicago Lying-In Hospital on Dec. 13, 1936. She appeared normal at birth, weighed 3,015 gm. and measured 50 cm. in length. Both parents were American born, non-Semitic, and in good health except for a history of renal glycosuria on the part of the mother. There had been no other children and no miscarriages nor stillbirths. There was no family history of deaths from splenomegaly with neurological signs in the first year of life.

The baby did well in the hospital and was discharged on Dec. 22, 1936, weighing 3,250 gm. Shortly after she was taken home, the parents noticed that she tended to keep her neck retracted and had a slight squint. She continued to gain weight, however, and at the age of 2 months, up to which time she had been breast fed, weighed 5,000 gm. Towards the early part of the third month, after she had been weaned because of insufficient breast milk, the infant began to take feedings poorly; the amount taken at each feeding decreased to about 2.5 oz. whereas previously she had taken 5 to 6 oz. At times she choked and had attacks of difficult breathing unassociated with intake of food.

On Mar. 2, 1937, the baby was brought to the Infant Welfare Clinic of the Bobs Roberts Hospital because of a cold, difficulty in feeding, and constipation. The parents also inquired as to the strabismus and the tendency to keep the head retracted. Examination showed pallor, a slight strabismus, and a palpable spleen (one to two fingers below the costal margin). No definite neurological manifestations were observed. The weight was 4,300 gm. The blood examination revealed the hemoglobin to be 40 per cent (Sahli), leucocytes 5,300 with a differential picture of 19 per cent neutrophils, 72 per cent lymphocytes, 7 per cent monocytes, and 2 per cent eosinophils. The urine was negative. The child was given iron for the anemia, steam inhalation and nasal drops, and the formula was changed. The patient returned on April 10, 1937, unimproved, with a definite retraction of the neck and opisthotonus. She looked pale and showed a pronounced convergent strabismus. The spleen was very large and the liver also palpable (two fingers below the costal margin). Hospital admission was advised.

Physical Examination.—On admission (April 13, 1937) the patient was found to be an undernourished white female infant weighing 3,900 gm. and with a tendency to keep the head retracted and the back arched in opisthotonus (Fig. 1*B*). It is noteworthy that the neck could be bent forward without difficulty. The arms were elevated to the level of the shoulder with flexion at the elbow and adduction, so that the hands fell into position over the lower part of the face (Fig. 1*A*). The legs were in a position of flexion. The infant tended to maintain these positions for long periods of time. She did not appear acutely ill, and the temperature was entirely normal. The skin had a pasty pallor; there were no eruptions or desquamations. The head measured 38 cm. in circumference. The anterior fontanel was open (2 by 3 cm.), and there was no separation of the cranial sutures. The ears were negative. Examination of the eyes showed a convergent strabismus with a rapid fine nystagmus. The pupils reacted well to light and the fundi were normal. The child appeared to perceive light but did not follow objects with her eyes. There

was no facial asymmetry, but the expression was peculiar. The nose, mouth, and throat revealed no significant findings. The cervical lymph nodes were moderately enlarged. The chest was symmetrical, the lungs clear, and the heart normal. The abdomen was not distended, even though the liver was enlarged two fingerbreadths below the costal margin and the spleen reached down to a centimeter above the left iliac crest. The splenic notch could be felt plainly; the organ was firm to touch and extremely movable. There was a reducible protrusion of the umbilicus. The genitals were normal. The deep reflexes were brisk but not definitely increased. There was no clonus, but the lower extremities were slightly spastic. The plantar reflexes were both in extension. The Oppenheim sign was positive. Abdominal reflexes could not be elicited.



A. *B.*

Fig. 1*A* and *B*.—Photographs of patient taken soon after the first admission. The shaded area represents the palpable portion of the liver and the dotted area that of the spleen.

Laboratory Findings.—The blood count was 65 per cent hemoglobin (Sahli), erythrocytes 4.85 million, and leucocytes 11,600, the latter giving the differential count of 46 per cent neutrophils, 46 per cent lymphocytes, 3 per cent monocytes, 4 per cent eosinophils and 1 per cent basophils. No nucleated red cells were seen in the peripheral blood. A tuberculin test (Mantoux) was negative, as were also the Kahn and Wassermann tests. The spinal fluid, containing two to three cells (lymphocytes) per cubic millimeter, was clear, under no increased pressure, and there was no increase in globulin content. The urinalysis was negative. Roentgenography of the long bones revealed no abnormalities.

At this stage of observation it occurred to the authors that the case probably belonged to one of the groups of lipoidosis. While in the hospital the patient was unable to swallow food properly, taking no more than 2.5 oz. of formula at one

feeding (a total of 500 c.c. daily). On April 15, 1937, a slight dullness was noted with diminished breath sounds over a portion of the right lower lung, and a roentgenogram of the chest taken at this time revealed a pneumonic infiltration extending outward from the right hilum. The following morning the patient developed a fever of 39° C. Daily hypodermoclysis was then instituted, and with the aid of two blood transfusions the temperature dropped to the normal level within ten days. During this period of febrile attack the patient had occasional spells of transient cyanosis. Blood cholesterol was then determined and showed to be 129 mg. per cent, which argued against the possibility of Niemann-Pick's disease. A sternal marrow puncture (Kato[20]) was performed on April 26, 1937, and the smears made from the aspirated material contained characteristic Gaucher cells (Fig. 2) which constituted conclusive proof of Gaucher's disease (infantile type).

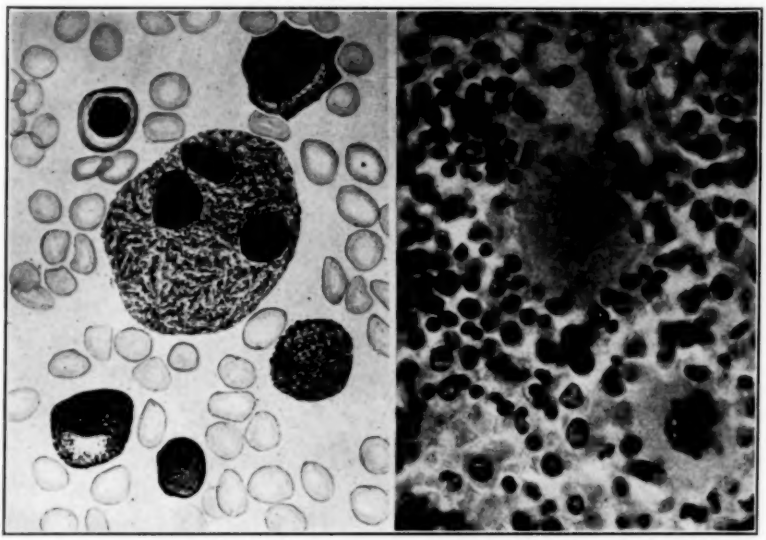


Fig. 2. Fig. 3.

Fig. 2.—Camera lucida drawing of a Gaucher cell seen in the smear made from sternal marrow puncture material. Reduced from magnification of 1300 diameter. May-Grünwald-Giemsa stain.

Fig. 3.—Photomicrograph of a section of bone marrow showing a Gaucher cell and a megakaryocyte.

At the request of the parents the patient was taken home on April 28. Her weight was then 3,900 gm. While at home the baby took hardly any food or fluids, had a few attacks of laryngeal spasm, and was extremely restless. Two days later, cyanotic and pale, she was brought back to the hospital in a precarious condition. Her tissue turgor was very poor, the fontanel was sunken, and the respiration, labored. The weight decreased to 3,500 gm., but with daily hypodermoclysis and repeated intravenous administration of fluids her condition considerably improved. Gastric gavage had to be resorted to because of her inability to take food, after which the body weight increased to 4,305 gm. in six days. The blood count at this time was 59 per cent hemoglobin (Sahli), erythrocytes 4.84 million, and leucocytes 5,600, with a differential count of 26 per cent neutrophils, 66 per cent lymphocytes, 2 per cent monocytes, and 1 per cent each of eosinophils and basophils. The urinalysis was completely negative. On the seventh day, after an attack of diarrhea and an elevation of temperature up to 39.8° C., the infant, while being fed, suddenly became cyanotic and her respiration stopped abruptly (May 7, 1937).

Autopsy Protocol.—Autopsy, which was restricted to inspection of organs and removal of only necessary tissues through an abdominal incision, was performed by Dr. Humphreys and Dr. Steiner about seven hours after death and resulted in the following anatomic diagnosis:

(1) Lipoid histiocytosis, Gaucher type, with extreme splenomegaly and moderate enlargement of the liver; (2) lipoid storage in the lungs, lymph nodes, thymus, adrenal glands, bone marrow, and lymphoid tissue of the intestine; (3) acute bronchopneumonia; (4) hemorrhages in serous membranes; (5) emaciation; (6) excoriations on the buttocks and scalp.

The gross appearance of the liver and spleen was most remarkable. The liver (not removed) was estimated to weigh at least twice the normal for a child of this age. The capsule showed much irregular purple-red and yellow-gray mottling, coarser than normal lobular markings. The margins were strikingly rounded. Upon incision

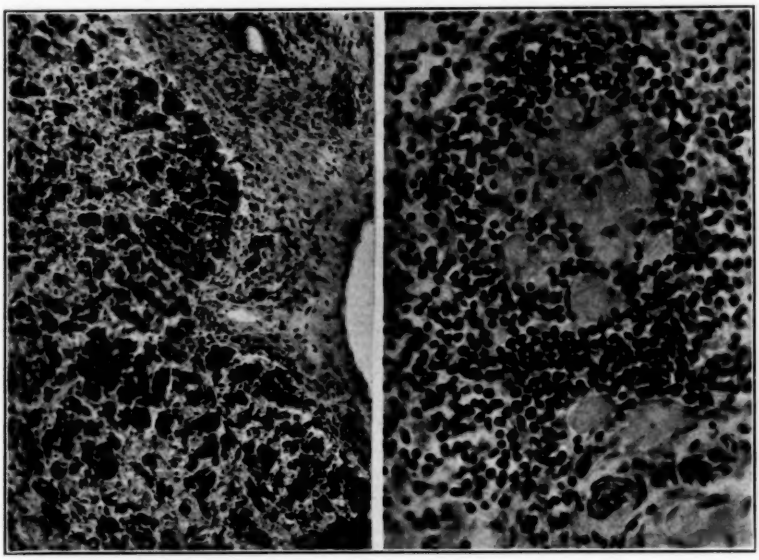


Fig. 4. Fig. 5.

Fig. 4.—Photomicrograph of a section of liver, showing atrophy of liver cells due to accumulation of Gaucher cells.

Fig. 5.—Photomicrograph of a section of spleen, showing accumulation of Gaucher cells in the center of a small Malpighian corpuscle.

of the organ, bulging and very friable liver tissue protruded, to the extent that the organ was practically diffluent.

The spleen was an enormous soft organ weighing 110 gm. (seven times the normal), with delicate capsule. The splenic pulp which bulged forth upon incision of the capsule was uniformly pale purple red with no recognizable lymphoid bodies.

The most characteristic feature of the case was the histologic demonstration of ubiquitous presence of Gaucher cells, which were found in great abundance in the spleen, liver, thymus, lungs, lymph nodes, and in the lymphoid tissue of the intestines (Peyer's patches) and appendix, bone marrow, adrenal glands, and in moderate abundance in the kidneys (Figs. 3 to 7).

Histologic Characteristics of Gaucher Cells.—The Gaucher cells seen in this case were typical of those described in the literature: huge, pale cells, sometimes multi-

nucleate and only occasionally definitely vacuolated. More frequent was the appearance of wrinkling or striping of the cytoplasm, well brought out by the Maximow and Mallory stains. Here too the cytoplasm was of a dingy grayish or brownish cast, quite in contrast to the other mononuclears. Foot silver stains failed to demonstrate any increase of reticulum. Scharlach R brought out no evidence of neutral fat or lipoid in any section, except in the adipose tissue cells (liver, spleen, kidney, lung, lymph node, bone marrow). With modified Weigert stains (Lorrain Smith-Dietrich) the only tissue in which lipoids could be unequivocally demonstrated was in the adrenal cortex; here Gaucher type cells, free from granules, surrounded by adrenal cortical cells packed with blue and blue-black coarse and fine granules, were definitely identified. Thus the fat stains strikingly demonstrated the absence of any chemically

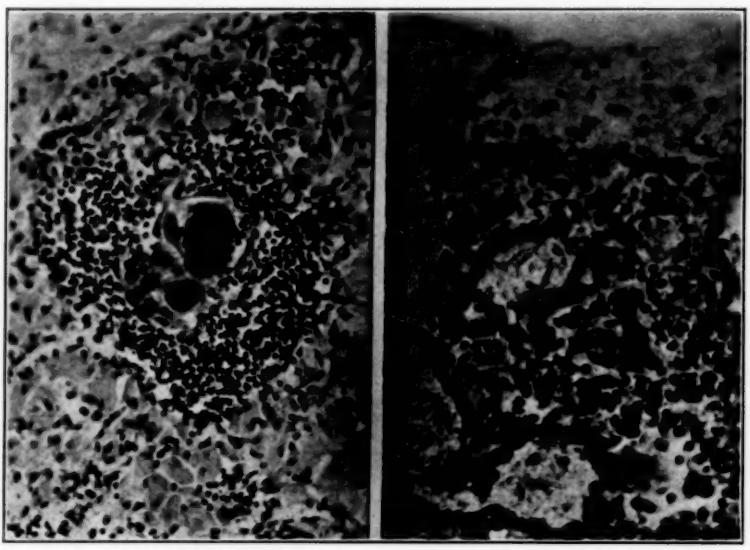


Fig. 6. Fig. 7.

Fig. 6.—Photomicrograph of a section of thymus, showing dense accumulation of Gaucher cells around a lymphoid follicle.

Fig. 7.—Photomicrograph of a section of lung, showing accummulation of Gaucher cells beneath the visceral pleura.

active lipoids (found in abundance in Niemann-Pick's disease where phospholipins abound), as well as the scarcity of sudanophilic fat and lipoid.* No granular iron was recognizable in the hematoxylin-eosin sections.

*Chemical analysis of the liver and spleen (Dr. Marberg) revealed the following values for various lipoids:

	LIVER	SPLEEN
Weight of sample used	81.0 gm.	72.0 gm.
Weight lipoidal extract	4.57 gm.	4.84 gm.
Weight of extracted dry residue	12.2 gm.	9.4 gm.
Total solids	16.6 gm.	14.2 gm.
Ratio total lip. total sol.	27.2%	34.0%
Free cholesterol		
Total cholesterol	66.0%	85.5%
Percentage of total lipoids		
Free cholesterol	4.5%	5.6%
Cholesterol ester	1.2%	1.6%
Phosphatides (as lecithin)	44.9%	30.6%
Cerebroside (as kerasin)	43.6%	36.6%
Balance, neutral fat plus fatty acid	5.8%	25.6%

ETIOLOGY

Cases of Gaucher's disease have been reported in every age period from infancy to old age. Attention has already been directed to the relatively large percentage of cases (more than one-sixth) in which the disease took its onset during the first year of life. In some instances evidence of its onset was even noted very shortly after birth. Kohn,[22] for example, found an infant during its first week of life to have an enlarged spleen, and in the case presented here the parents first noticed retraction of the head and strabismus on the ninth day of the child's life. Inasmuch as it seems logical to infer that before the typical symptoms appear, there must be a relatively extensive infiltration of organs by the pathologic cells, these cases bespeak a congenital origin.

The positive familial tendency of this illness has long been recognized. Rettig[38] and Bychowski[8] have reported cases in children and in the parents of one of them. Anderson[2] observed the disease in the first and third generations. Upon these grounds Bloem, Groen and Postma[5] suggest the recessive characteristic of the disease to be hereditary.

At one time it was supposed that females were affected more frequently than males. But in the infantile cases, summarized in Table I, the distribution as to sexes is about equal, in conformity with which the majority of authors consider there to be no significant sex predisposition. As to race there seems to be a much greater incidence in the white race; but contrary to the commonly accepted belief, the Jewish race shows a special predilection to Gaucher's disease. Cases have been reported in practically every race. The disease is also said to be very common in India, as observed by Spackman and Mackie.[43]

Along with most diseases of obscure origin, tuberculosis and syphilis have been regarded by some as etiologically related to Gaucher's disease. But the majority of cases on record have manifested no evidence of Koch's infection, and tuberculin and Wassermann tests have usually been negative.

PATHOGENESIS

The nature of the disease is still imperfectly understood. Gaucher,[15] in describing the first such case, regarded the condition as neoplastic, but Bovaird[7] denied such a possibility. Schlagenhaufer[42] based the disease on a systemic affection of the reticulum cells of the lymphatic and hematopoietic organs. Simultaneously, Marchand[28] stressed the significance of deposits of foreign material commonly found in the histogenesis of the Gaucher cell. In 1915 Mandelbaum and Downey[27] traced the origin of this cell to the reticulum of the lympho-hemopoietic organs. Later Pick[34] showed that they originate as well from the histiocytes of the arterioles of Glisson's capsule and from the periadventitial cells of the capsular vessels and central veins. With the aid of silver stains Pittaluga and Goyanes[35] uncovered further evidence of such sites being the origin of the Gaucher cell.

In infants Gaucher cells occur in unusual locations, a deviation partly explained by the differences between the development of the reticuloendothelial system of infants and that of adults. Epstein[13] and Lieb[24] were the first to identify the substance accumulated in the Gaucher cell as a complex cerebroside kerasin, an observation later verified by numerous other workers. Chemical determinations of the spleen have given variable results. Bloom and Kern[6] found no changes in nitrogen, phosphorus, cholesterol and fatty acids, but low values for these substances were reported by other workers. Metabolic studies in patients of various ages have also been inconclusive. Cholesterol, fatty acids, and phospholipids in the blood have been found by some to be low in values, and by others, normal. In infants, few of these substances have been determined except cholesterol, and that has been found to be consistently low in value. Phosphorus and calcium estimations, carbohydrate, and nonprotein nitrogen have all been invariably normal, and the spinal fluid uniformly negative.

Attempts to produce the disease experimentally have not as yet been successful, but the work of Beumer and Gruber[4] may lead to profitable findings in this field; these authors have reproduced the changes characteristic of Niemann-Pick's disease by injections of large amounts of sphingomyelin, the substance specifically concerned in this disease. When Beumer and Gruber used lecithin-cephalin, in place of sphingomyelin, no results were obtained. It is significant to mention that kerasin is chemically related to sphingomyelin, both containing sphingosine in their nucleus. The changes in the spleen observed by Babes,[3] after continued coal tar painting of rabbit's skin, closely simulate the essential pathology seen in Gaucher's disease, but a chemical confirmation of the storage substance is lacking.

As concerns the cause of Gaucher's disease the theory most widely accepted at present, and one upheld by Pick, is that the condition arises from an overloading of certain active elements of the reticulo-endothelial system with large quantities of kerasin, which in turn accumulates because of an abnormality of lipoid metabolism. Thannhauser[45] goes one step further and suggests that kerasin is produced at the expense either of sphingomyelin or of sphingosine normally present in the body.

PATHOLOGY

Pick outlined the major pathologic features of Gaucher's disease and clearly distinguished it from Niemann-Pick type of lipoidosis. In infants the spleen, liver, lymph nodes, and bone marrow undergo the chief outstanding gross changes. But the distinctive feature of the disease is the Gaucher cells, large (20 to 80 microns in diameter), pale polygonal cells with a homogeneous and opaque cytoplasm when observed in the fresh state. The nuclei are relatively small, hyperchromatic, and eccentrically placed; occasionally they are multinuclear.

With Mallory's stain a delicate network of dark blue wavy or straight lines can be observed, accentuating the wrinkled appearance of the cell; between these wrinkles the protoplasm appears pale blue. In Gaucher cells from adult patients Turnbull's reagent sometimes gives a faintly positive reaction for iron in the cells, and one of the striking features of these cells is their failure to give the usual reactions for fats and lipoids. In contrast to the orange coloration assumed by the Niemann-Pick cells, after mordanting with potassium bichromate, Gaucher cells stain very pale yellow with sudan III. Similarly, with nile blue sulfate only a light blue color is obtained. Anisotropic bodies rarely appear.

In the spleen and in lymph nodes Gaucher cells tend to collect in clusters presenting typically alveolar arrangement of cell nests, a phenomenon not observed in all organs. True to type they are most numerous in the spleen, lymph nodes, bone marrow, and liver, in which latter location they are found in the capillaries; in the marrow, compressed by the neighboring cells, they tend to be elongated and spindle-shaped. In addition to the above locations Gaucher cells have been found in the lungs, the suprarenals, and in the lymphatic reticulum of the intestines and tonsils. In infants these cells are less abundant and more widely scattered than in adults. These findings have been verified in the present case.

In the central nervous system the findings are unique, as pointed out by Jenny[19] and by Oberling and Woringer.[33] No typical Gaucher cells have ever been found here. Except for scattered gliosis under the ependyma of the third ventricle, the pathology is restricted to the pyramidal (large and small) cells of the cerebral cortex. The lesions are the most widespread in the occipital and parietal regions but are found throughout the cortical substance. With ordinary stains the pyramidal cells are sharp of outline. The ganglion cells are so retracted as to appear "densified" or "mummified," and the contours are angular. With Nissl's stain the cytoplasm is seen to be modified by a conglomeration of the tigroid substance in a chromophilic mass filling a large portion of the cell body and involving a part of the processes. This almost conceals the nucleus. Many of these cells contain vacuoles of variable sizes, some large enough to distend the cell bodies. There is no neuronophagia, and no pathologic changes have been found in the brain stem.

SYMPTOMATOLOGY AND DIAGNOSIS

From the summary of symptoms observed in various cases of Gaucher's disease (Tables I and II) it is readily evident that when this disease sets in before the age of 6 months, neurological findings are likely to be the outstanding factor. These cases set in, for the most part, with dyspeptic manifestations and failure to gain in weight, together with

more or less indefinite additional symptoms indicative of generally failing health. By the time this stage is reached, the spleen is usually moderately enlarged, and as this organ then progressively increases in size, hepatomegaly gradually becomes apparent. The neurological syndrome usually appears after the onset of the splenic enlargement. Retraction of the head, opisthotonus, and strabismus are the earliest signs of the neurological syndrome, followed by the development of laryngeal spasms, dysphagia, and spastic extremities with changes in the reflexes. The limbs are often maintained in the same position for prolonged periods, commonly referred to as catatonia. The patient assumes the characteristic position of elbows flexed, forearms adducted and slightly pronated, and hands held in front of the face. In most cases the legs are kept in flexion (Figs. 1*A* and *B*). The expression on the baby's face is one of peculiar sadness, and the infant rarely shows any awareness of its surroundings. In some cases, in a later stage of the disease, complete loss of sensation and even idiocy may ensue.

The course of the disease is accompanied by a gradual but steady loss of weight and arrest of physical and mental development. A slight anemia with leucopenia is frequently observed. The blood cholesterol is likely to be diminished. Off and on the temperature is elevated, the cause being undetermined except possibly in one case in which the fever appeared to coincide with low fluid intake. Finally within a few months' time the infant reaches a marantic stage, in the course of which he succumbs either to an intercurrent infection or as a result of the cachexia itself. In some instances death has occurred during a laryngeal spasm at any stage of the disease.

In cases in which the disease process begins after six months of age, neurological manifestations as a rule do not develop, the first evidence of the disease being only the definite symptoms of generally failing health. But soon thereafter the abdomen noticeably and rapidly enlarges; the spleen increases in size, followed by hypertrophy of the liver. A moderately severe anemia produces pallor. The course, although not as acute as in the younger group, is rapid and the immediate cause of death is most likely to be cachexia and intercurrent infection. Splenectomy may precipitate the termination.

It is noteworthy that in Gaucher's disease of infancy certain of the symptoms so frequently found at a more advanced age are rarely encountered. Pinguecula-like deposits on the conjunctivae and large brownish pigmentations of the skin have never been reported in infants suffering with the disease, although an ocher cutaneous discoloration may be seen. Hemorrhagic tendencies may become manifest during the second half of the first year, but bone involvement, at least as far as roentgenographic evidence is concerned, practically never occurs.

It must be added that neurological manifestations in Gaucher's disease are not wholly confined to infantile cases; they have also been observed

in some older patients with Gaucher's disease, such as the case reported by Hoffman and Makler and those observed by Reiss and Kato. In the patients reported by the latter authors, neurological symptoms appeared long after the onset of the disease, at a time when hemorrhagic manifestations were prominent. In the absence of postmortem studies the plausible assumption is that the symptoms referable to the nervous system in these cases have been produced by hemorrhages, as at the time diagnosed, rather than being the result of the pathologic background of the nervous symptoms in the infantile form of Gaucher's disease.

DIFFERENTIAL DIAGNOSIS

If the neurological symptoms are pronounced and typical, the diagnosis of Gaucher's disease is not difficult to make on clinical basis alone. But in all other cases the proof of positive diagnosis must be derived from laboratory procedures (sternal and splenic punctures). The neurological form has to be differentiated from: (1) congenital syphilis, (2) cerebral agenesis, (3) erythroblastosis neonatorum, (4) Wilson's disease, and (5) Niemann-Pick's disease, including amaurotic family idiocy.

Congenital syphilis is ruled out by the absence of the usual symptoms and indications of syphilis, and by negative serology. The diagnosis of cerebral agenesis should be made only on the basis of elimination of other diseases. Even though an infant with glaring congenital defects in the brain is likely to be more predisposed to secondary anemias than is a normal baby, the enlargement of the spleen and liver is a signal conspicuous enough to arouse suspicion and, unless satisfactorily explained otherwise, diagnostic punctures should be performed. Erythroblastosis of the newborn infant may also cause an enlargement of the liver and spleen, attended by neurological findings, but the latter symptoms are usually in the nature of true paralysis or of generalized convulsions; moreover, erythroblastosis is frequently accompanied by jaundice, hydrops, and hemorrhagic tendencies, which do not occur in the neurological form of infantile Gaucher's disease. The blood study would settle the diagnosis beyond any doubt. Wilson's disease practically never occurs at this early age. But the greatest difficulty encountered in the differential diagnosis of Gaucher's disease is in distinguishing it from Niemann-Pick's lipoidosis. The more important points of contrast between these two diseases may best be tabulated in Table II.

In cases free of a neurological syndrome, the positive diagnosis can be made only from the characteristic cytology of the biopsy tissues, such as the sternal marrow, spleen and lymph node punctures. This group of Gaucher's disease has to be differentiated from: (1) syphilis, (2) Niemann-Pick's disease, (3) hemolytic icterus, (4) erythroblastic anemia of Cooley, (5) anemia pseudoleucemia infantum of von Jaksch, (6) adrenal neuroblastoma of Pepper type, (7) Letterer-Siwe's disease,

TABLE II

	GAUCHER'S DISEASE (NEUROLOGICAL FORM)	NIEMANN-PICK'S DISEASE
1. Age of onset	First six months	May begin after six months
2. Race	No special predisposition	Jewish race (50%)
3. General appearance	Usually no discoloration of skin; expression of sadness	Mongoloid facies frequent; discloration of skin usually
4. Neurological	Hypertonia; strabismus; laryngeal spasm; dysphagia; catatonia	Usually hypotonia; no pseudobulbar syndrome
5. Liver and spleen	Splenomegaly usually precedes hepatomegaly	The opposite may be found
6. Fundi	Negative; occasionally temporal pallor	Cherry red spot or pigmentation at macula lutea frequent
7. Blood	Slight anemia and leucopenia; no morphologic changes	More severe anemia with leucocytosis; vacuoles in the cytoplasm of lymphocytes frequent
8. Chemistry	Normal or low blood cholesterol and fatty acids	All these are definitely elevated
9. Biopsy	Relatively scarce presence of Gaucher cells in the sternal marrow, but numerous in splenic tissue	Relatively numerous Niemann-Pick cells in all aspirated tissues

(8) Banti's syndrome and, in tropical countries, (9) malaria, and (10) kala-azar.

But in each of the above conditions the characteristic Gaucher laboratory findings, particularly the absence of the Gaucher cells in the biopsy materials, are consistently missing.

COMMENT

A review of the literature on infantile Gaucher's disease discloses unmistakable evidence of a definite relationship between the age of onset of the disease and its clinical manifestations. As Reuben and Rowland emphasized, when the condition sets in during the first year of life, the course is almost always very rapid. It is furthermore to be noted that in cases of infantile Gaucher's disease developing before 6 months of age, as in the present case, a striking neurological syndrome is encountered, as well as pathologic changes in the cerebral cortex of a nature different from the usual findings of the disease (absence of true Gaucher cells). In addition the Gaucher cells themselves seem to overflow the usual boundaries and permeate the thymus, tonsils, suprarenal medulla, the lymphoid tissues of the intestinal tract, and even the lungs. In contrast to this, in cases beginning in the second half of the first year, the morbid anatomy is limited to the usual organs (spleen, liver, bone marrow, and lymph nodes), and the resultant clinical picture

is merely characterized by enlargement of the liver and spleen and a moderately severe anemia. But in either instance the disease proceeds rapidly to fatal termination.

This swift course no doubt accounts for the absence of such chronic manifestations as pingueculae and bone changes, as well as for the diminished incidence of hemorrhagic tendencies. As there is but a slight variance in the acuteness of the process in both groups, it seems unlikely that the severity of the disease would in itself account for the great differences in the extent of the pathologic involvement. As Pick[34] suggests, it is more likely the particular stage of development of the reticuloendothelial system, in the individual case, which is responsible for these variations in pathologic picture among the numerous cases of Gaucher's disease. With the exception of the cerebral changes this statement is strongly supported by the work of Lubarsch,[25] whose investigations on the phagocytosis of iron pigment and fat in infants have shown that the phagocytic tendency undergoes a definite change towards the end of the first year of life. By that time cells hitherto capable of storage lose their capacity of phagocytosis. Among these cells Lubarsch included the reticulum cells of the thymus and the perivascular cells of the suprarenals and tonsils. Significantly enough, these are practically the same groups of cells that are specifically affected in the Gaucher's disease of early infancy.

Regarding the central nervous system no satisfactory explanation of the atypical pathology can be offered. But, in harmony with the view advanced by Meyer,[29] it may be assumed that the factor determining the pathologic changes is the peculiar substratum of the developing infantile cerebral cortex. It is universally accepted that active development of this portion of the nervous system takes place during the first year of life. Further studies in this field need to be undertaken with a view to uncovering important information on the relationship of different brain cell groups to the reticuloendothelial system.

SUMMARY AND CONCLUSIONS

The literature on Gaucher's disease in infancy has been reviewed, and a new case reported.

The cases reviewed fall into two rather sharply distinguishable groups: (1) those in which the disease begins before 6 months of age, and (2) those in which it begins after 6 months of age.

In the first group of cases, of which the present case is an example, neurological manifestations are frequently observed, while in the second group they are rarely encountered.

In view of the fact that in both forms the disease follows a rapidly fatal course, the differences between them in clinical manifestations and

in pathologic findings can be explained only by the difference in distribution, and perhaps by functional variations, of the reticuloendothelial elements at different periods of infancy.

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THE TREATMENT OF GONORRHEAL VAGINITIS WITH CORBUS-FERRY GONOCOCCUS FILTRATE

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DESPITE a wide variety of empiric methods and new suggestions of treatment we are still struggling with gonococcus infections, one of the most resistant and age-old affections afflicting humans. Stockwell[1] holds that gonorrhea existed thirty-six centuries before Christ and was observed by Juvenal, Persius, and Galen. Efforts at cure still continue by new and old methods. While recent research devoted to the treatment of gonorrheal vaginitis with estrogenic substances is in process of development, the use of gonococcus filtrate for the condition has come to the fore. Controversial evidence seems to indicate that evaluation of these newer therapeutic agents awaits further corroboration in order to be established as superior to the local remedies. This study on treatment by Corbus-Ferry filtrate* was undertaken to determine the efficacy of the method in a group of twenty-four children with gonorrheal vaginitis.

In order to appreciate the variety of approaches to combat the disease it is necessary to recall that gonococci can be acted upon in two ways, as pointed out by Ernest Finger,[2] either directly by destroying them or indirectly by producing a change in their soil, that is, rendering the mucous membrane unfavorable to their proliferation. Treatment by filtrate is an example of the first method, that by estrogenic substances, of the second method. Chemical destruction of the gonococcus has yielded uncertain results because no chemical agent as yet available kills the submucosal bacteria.

The beginning of the method of producing counteraction to overcome the inroad of the gonococcus is traceable to the middle of the nineteenth century. It was Pasteur who laid the foundation of the present activities, the principal factor being the production in bouillon filtrate of a substance called the antivirus. As early as 1897 the first attempts at dealing with a gonococcus toxin were reported by de Christmas.[3] The opinion is that he used autolyzed cultures containing appreciable amounts of endotoxin. Herrold,[4] in 1925, did some important experimental work, obtaining a filtrate from cultures of the gonococcus.

Since we are concerned with the effectiveness of a bouillon filtrate containing antivirus it would be well to define the meaning of this

*We are indebted to Parke, Davis & Company for supplying us with the material for the treatment of these patients.

term. An antivirus, as described by Corbus and O'Conor[5] is an atoxic, nonantigenic, thermostable substance, formed in culture media, which is easily detached from the body of the bacterial cells and is antagonistic to them. It is more abundant in the liquid media when all the bacterial cells are dead or incapable of continued proliferation. The antivirus is said to cause the death of the bacteria in the culture medium. Besredka found that the action in vitro could be produced in vivo. To exert its specific activity the antivirus must come in contact with the bacteria.

Corbus, stimulated by the work of Besredka in specific immunization by antivirus, directed his attention to the possibility of producing a gonococcal antigen solution. After prolonged experimental work he and O'Conor[6] succeeded in producing a bouillon filtrate of the organism. The bouillon developed by them at this time was toxic and antigenic. After a thorough trial of intra-urethral injections in eighteen cases by Corbus and O'Conor, the results proved discouraging. The assistance of Dr. N. S. Ferry was requested by Corbus in making a new preparation. In the fall of 1929, Clark, Ferry, and Steele,[3] using a hormone broth, produced a gonococcus bouillon filtrate and discovered that it contained a soluble toxin and was not an antivirus. This gonococcus filtrate proved a difficult problem in analysis because of lack of adaptability to artificial conditions of culture and the inherent tendency of cultures of gonococcus to autolyze. In dilutions of 1:1,000 and 1:1,500 the toxin was found capable of causing skin effects similar to the Dick reaction. In experimenting with animals it was further revealed that this toxin stimulated the formation of an antitoxin which neutralized in vitro as well as in vivo. Using this new preparation by Ferry, Corbus and O'Conor injected it intradermally in two patients. Their results encouraged them to believe that intradermal injections of gonococcus bouillon filtrate, properly controlled, brought about specific immunizing effects destructive to the organism in most instances.[7]

In vivo bacteria are lodged in certain tissues or cells. In the application of the antivirus-containing filtrates the biologic fact that skin cells are capable of producing immunity has been utilized. In other words, they found that the antigenetic response from some toxins, if given intradermally, seems to have the power of inducing general immunity for their respective bacteria. It is generally believed that every virus has its cell and every cell its immunity. But such local immunity forms only a part of the general immunity which can be stimulated by intradermal injections introduced anywhere in the body.[8]

Corbus and O'Conor[7] later observed that by withholding all other therapeutic methods they could influence the course of the disease

favorably in acute cases but that the rapidity of the cure did not always exceed that attained by means of medicaments. Treatment of eight women with gonorrheal endocervicitis yielded most encouraging results. In three young girls with vulvovaginitis of specific origin the outcome was equally promising. They felt that in some persons at least the gonococcus was eliminated permanently by these injections alone.

In 1932 Corbus again reported on the results of treatment with filtrate in a series of 151 male patients with gonorrheal infection.[9] Other investigators (McKay, Storts, Stockwell, Townsend, and Spence)[10] also sought to determine the effectiveness of this type of therapy. The Council of Pharmacy and Chemistry of the American Medical Association made two preliminary reports,[11] both times awaiting further evidence of the clinical value of the Corbus-Ferry filtrate. A recent survey of a number of urologists regarding their opinion of this product, based on actual trial, showed that with but few exceptions, its use has been discontinued either because of lack of therapeutic results or the too common precipitation of serious complications after its administration.[12]

Experimental observations, however, continued, with both favorable and unfavorable results (Jamieson, Deakin, Gardner, Whitehouse, and Anwyl-Davies).[13] After further consideration the Council of Pharmacy and Chemistry made its final report,[14] declaring that the Corbus-Ferry gonococcus filtrate is not acceptable for new and nonofficial remedies. In the meanwhile we had undertaken our investigation.

PRESENT CLINICAL STUDY

A series of twenty-four consecutive cases of gonorrheal vaginitis in children at the Essex County Hospital for Contagious Diseases, at Belleville, New Jersey, was made the subject of intensive study. Each child had a history of vaginal infection, associated with a purulent discharge, burning, and itching. The clinical experiment to determine the therapeutic value of Corbus-Ferry gonococcus filtrate in the treatment of this disease was begun on June 9, 1936, and terminated on July 13, 1937. The ages of the children ranged from 2 to 10 years. The duration of the gonorrheal infection in these patients before institution of the new form of therapy varied from eleven to seventy-nine days.

Previous treatment by local antiseptics had been given over a period varying from one to fifty-four days. In most of the cases it consisted of argyrol, 10 and 20 per cent twice a day, instilled locally, followed by a potassium permanganate douche of 1:8,000 twice a day. Some of the children were given a 2 per cent boric acid douche, followed by application of metaphen ointment (⅕ of 1 per cent) tri-weekly.

In all cases the employment of local medicaments was supplemented by hygienic measures.

For the purpose of ascertaining if the results in the types of gonorrhea would differ, the cases were divided into two groups: acute and chronic. This classification was made arbitrarily, the disease of a duration of forty days or less being considered acute and over forty days, chronic. The entire number consisted of fifteen acute cases and nine chronic cases. All patients originally showed positive gonococcus smears, that is, the presence of gram-negative intracellular diplococci of morphologic resemblance to gonococci, which is the criterion for the diagnosis of gonorrheal infection. In all but two cases the smears were positive for gonococcus at the beginning of the experimental therapy with the filtrate. These two patients, in whom the discharge had not cleared up by previous local treatment, were included in the series to determine the effect, if any, of the new treatment on the presence of the discharge. Their smears contained pus, but no microorganisms could be isolated.

The children were given varied dosages of the Corbus-Ferry gonococcus filtrate intracutaneously with the purpose of determining the optimum dosage. In eight cases the dosages given twice weekly ranged as follows: 0.0083⅓, 0.1, 0.075, 0.1, 0.125, 0.15, 0.175, and 0.2 c.c. In fourteen cases, from 0.01 to 0.02 c.c. of the filtrate were given twice weekly. Two patients received a bi-weekly constant dosage of 0.01 c.c. Judging from the response to the varied dosages we found that the smaller the dosage the better was the result. Probably a dosage in the neighborhood of 0.01 c.c. of Corbus-Ferry gonococcus filtrate given intracutaneously twice weekly is the optimum for use in children with gonorrheal vaginitis.

Regarding local reactions from filtrate injections, these varied from none whatsoever, which happened in a few instances, to cutaneous wheals of 50 to 75 mm. in twenty-four hours. In rare instances, in which there was an absence of any local reactions, they occurred in the latter part of the disease. These reactions did not tend to disappear as the patients became cured of the disease. In other words, there was no relationship between the presence or absence of a local reaction and the progress of the disease. In some instances (seven) a rise in temperature to a maximum of 101.6° F. was observed. These constitutional reactions appearing in variable periods of the disease showed no dependence on the strength of the dosage.

In a few cases, after the filtrate was given intracutaneously it caused an increased vaginal discharge. This was such an inconstant factor that no definite statement can be made in regard to it.

Previous to the institution of filtrate therapy the following diseases were present in association with the gonorrheal vaginitis: gonococcic

pelvic peritonitis (two cases), congenital syphilis (one case), chronic rheumatic endocarditis (one case), scabies (one case), ringworm of the scalp (one case), and scarlet fever (one case). During treatment with filtrate therapy two complications occurred, namely, cellulitis of the left leg (one case), and acute tonsillitis (one case).

Three postulates governed the clinical results of treatment, namely: (1) the cessation of vaginal discharge, (2) absence of pus cells, and (3) the disappearance of gonococci in the smears. Before the children were dismissed as cured we had evidence of 22 to 44 consecutive negative vaginal smears. The number of days before the vaginal discharge ceased varied from 22 to 149 days. Before consecutive negative smears were obtained the children were under treatment from 6 to 119 days.

In the eighteen cases in which the patients were considered cured at the hospital the duration of treatment with filtrate ranged from the shortest of 28 days to the longest of 165 days, before dismissal and commitment to follow-up at the Health Department centers. These cases were checked periodically up to Jan. 7, 1938. The average length of treatment resulting in cure was 73.44 days. It was found that of the eighteen patients cured by filtrate therapy, five had recurrences. The length of time after dismissal from the hospital without a recurrence varied from 180 to 508 days. Thirteen, or 54.17 per cent, of the twenty-four patients in the series have continued without trace of the disease.

Six patients, representing 25 per cent, whom we were unable to cure by means of this form of therapy, were treated over a period ranging from 93 to 165 days, with varied dosages twice weekly, without apparent improvement.

In the two cases in which the patients had a vaginal discharge but did not show a positive smear, the infection cleared up in one and recurred in the other.

It may be definitely stated that no complication followed as the result of treatment by gonococcus filtrate in any case under observation.

COMMENT

We realize that twenty-four cases do not comprise a large number on which to pass judgment concerning the value of any therapeutic agent. But the fact should be stressed that these patients were under close observation at all times, data were accurately recorded, and smears were taken and examined daily.

The question arises whether the duration of the infection or the type of case was a factor in the cure. Of our thirteen patients who continue to be without trace of the disease, six were acute cases, and seven, chronic cases. Of the five recurrences three were acute and two, chronic cases. Obviously the difference is not sufficient to war-

TABLE I

SUMMARY OF PATIENTS TREATED WITH CORBUS-FERRY FILTRATE

PATIENTS	AGE IN YEARS	DURATION OF DISEASE BEFORE NEW TREATMENT (DAYS)	DURATION OF OLD TREATMENT (DAYS)	TYPE OF OLD TREATMENT	DURATION OF NEW TREATMENT (DAYS)	DURATION OF TREATMENT BEFORE CONSECUTIVE NEG. SMEARS STARTED (DAYS)	DURATION OF TREATMENT BEFORE VAGINAL DISCHARGE CEASED (DAYS)	NO. OF CONSECUTIVE NEGATIVE SMEARS BEFORE DISCHARGE FROM HOSPITAL	TIME SINCE DISCHARGE FROM HOSPITAL WITHOUT RECURRENCE (DAYS)
H. W.	9	36	29	Argyrol, 20%, B.i.d.* $KMnO_4$ douche, 1:8,000, B.i.d.	165	Not cured; treatment stopped 11/20/36			
J. M.	4	26	1	$KMnO_4$ douche, 1:8,000, daily	165	102	92	28	R†
C. M.	2	48	24	Argyrol, 25%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	151	119	149	33	427
O. S.	6	22	12	Argyrol, 10% and 20%, B.i.d. $KMnO_4$ douche, 1:5,000 B.i.d.	95	66	77	32	481
M. T.	3	48	38	Argyrol 10% and 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	70	39	64	32	508
A. H.	7	38	33	Argyrol, 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	108	77	96	33	R
J. M.	10	15	1	$KMnO_4$ douche, 1:8,000, daily	130	Not cured; treatment stopped 11/20/36			
M. G.	7	13	3	Argyrol, 10%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	71	40	67	31	508
G. B.	4	76	24	Argyrol, 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	18	11	22	37	390

*B.i.d.: twice daily.

†R: recurrence.

‡These patients previously showed vaginal smears positive for gram-negative intracellular diplococci

TABLE I—CONT'D.

L. W.‡	4	69	27	Argyrol, 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d. Boric acid douche, 2%, followed by metaphen ointment, 1/5 of 1 %, tri-weekly	28	Last positive vaginal smear 11/12/37	22	32	387
Ma. W.‡	7	68	54	Argyrol, 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	28	Last positive vaginal smear 11/18/37	23	25	R
My. W.	7	79	38	Argyrol, 10% and 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d. Boric acid douche, 2%, followed by metaphen ointment, 1/5 of 1%, tri-weekly	89	72	90	24	318
A. T.	10	40	34	Argyrol, 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d. Boric acid douche, 2%, followed by metaphen ointment, 1/5 of 1%, one day	126	Not cured; treatment stopped 3/22/37			
M. S.	9	48	26	Argyrol, 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	44	60	89	39	R
E. W.	3	35	29	Argyrol, 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	114	Not cured; treatment stopped 3/22/37			
L. D.	9	38	29	Argyrol, 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	62	45	71	30	340
E. F.	7	31	51	Argyrol, 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	106	87	108	22	R
J. V.	3	39	33	Argyrol, 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	93	Not cured; treatment stopped 5/18/37			
L. F.	5	41	33	Argyrol, 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	132	88	134	47	196
M. H.	3	24	2	$KMnO_4$ douche, 1:8,000, B.i.d.	99	Not cured; treatment stopped 5/25/37			
W. M. M.	4	41	7	Boric acid douche, 2%, followed by metaphen ointment, 1/5 of 1%, tri-weekly	85	40	77	40	196
F. B.	7	19	1	Argyrol, 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	38	6	22	31	245
E. McG.	3	11	3	Argyrol, 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	91	51	70	43	180
M. K.	3	36	32	Argyrol, 10% and 20%, B.i.d. $KMnO_4$ douche, 1:8,000, B.i.d.	41	13	34	34	204

rant any other conclusion except that the effect of treatment by gonococcus filtrate is the same in acute as in chronic cases.

In the opinion of some investigators the filtrate is a means of reducing the possibility of complications and attaining a safe postinfectious period. Our study permits us only to point out that there were no complications following treatment by filtrate therapy in our cases of children with gonorrheal vaginitis.

In reviewing the literature on the use of gonococcus filtrate one is impressed by conflicting evidence in regard to its value. We can discern belief in the product as a worth-while discovery on a sound biologic basis and the hope of progress along this line. Others have expressed doubt and condemnation of its use. It is our opinion based on our experience that Corbus-Ferry gonococcus filtrate has some value, for 54.17 per cent of cures cannot plausibly be considered by us as accidental. But we hold that more scientific work is necessary and should be done before definite and absolute judgment is passed on the therapeutic value of the filtrate.

SUMMARY

Review of the literature on the treatment of gonorrheal infection by Corbus-Ferry gonococcus filtrate shows diverse and conflicting evidence of its therapeutic value.

The present study on the use of this therapeutic agent was undertaken in an attempt to determine the efficacy of the method in a group of twenty-four children with gonorrheal vaginitis.

Varied dosages of the filtrate, ranging from 0.0083⅓ c.c., initially, to 0.01 and 0.2 c.c. were given bi-weekly over a period of 28 to 165 days.

There appeared to be no difference in the results between the chronic and acute cases. Of the eighteen patients cured by Corbus-Ferry gonococcus filtrate, five had recurrences. Thirteen, or 54.17 per cent, of the twenty-four patients in the series continue to be without trace of the disease.

From our experience we are inclined to believe that further experimental work scientifically carried out is indicated before the value of gonococcus filtrate as a cure for gonorrheal infection can be definitely determined.

We wish to acknowledge our indebtedness to Dr. Rose Bass and Dr. Frank Giuffra for their assistance in checking the cases following the dismissal of the patients from the hospital.

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CELIAC DISEASE AND ITS ULTIMATE PROGNOSIS

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MORE than 150 articles on celiac disease have appeared in the literature during the past five years, but its etiology remains unknown. Thaysen[1] believes that tropical sprue, nontropical sprue, and celiac disease are identical, Parsons[2] believes otherwise. Some hold that carbohydrates are at fault,[6, 11] and some that it is the fats,[2a, 29] others believe it to be an avitaminosis,[38] and still others, an endocrine[3] disturbance.

In such a conflict of opinions the only criterion which can be satisfactorily applied is the result of therapy. Following, an attempt will be made to show there is no symptom pathognomonic of the disease, that the symptoms of celiac disease depend upon an intolerance of carbohydrates, that the fatty stools which are regularly present may be due to this fault, that it can be readily cured by a strict high protein-banana diet, from which other carbohydrates and plain milk have been excluded, and that the exclusion of fats[29] does not accomplish this.

Celiac disease, although first brought to attention by Gee[4] in 1888, was not known to the average physician until recent years.

Herter[5] in 1908 published a monograph on intestinal infantilism. His conclusions were that the tolerance for protein is excellent, for fats, variable, and for carbohydrates poor. This was the first step toward a correct understanding of the therapy necessary for the treatment of celiac disease. He also found a changed intestinal flora, the importance of which later investigators have minimized.

These observations were not given practical application until Howland,[6] in 1920, in a paper entitled "The Treatment of Prolonged Intolerance to Carbohydrate," advocated the use of a high protein, carbohydrate-free diet with limitation of the fats. His good results were later duplicated.[7]

At about this time I was fortunate enough to discover that ripe bananas, rich in carbohydrates, could be used in celiac disease with benefit, would supply all the carbohydrates required, and when added to a high protein diet regularly produced a cure.[8]

Although this treatment has proven successful in the hands of physicians in all parts of the world, there are still large numbers, especially among the English, who persist that the fats are at fault in celiac disease.

In 1931 Parsons,[9] in the opening remarks of his Ratchford Memorial Lectures, stated that "the outstanding feature in celiac disease is the inability of the child suffering from it, properly to absorb fat from the intestine," and ended with the statement[10] that "the treatment of celiac

disease is very tedious and full of anxiety because it is so prolonged, lasting sometimes for years, and progress is so slow; at times there are bad, even catastrophic setbacks, hence, unless there is hearty cooperation and the will to conquer on the parts of the parents and the doctor, success will never be achieved."

Thus, despite an unknown etiology, the difference in the results of treatment based on these hypotheses is striking and would seem to indicate that the symptoms depend upon an inability of the patient to utilize the usual carbohydrates.

Whenever a disease is described for the first time, it is natural that the severe cases which are outstanding should be the only ones recognized. This is what happened in the description of celiac disease, in which the anemic, irritable, stunted child with large abdomen, flat buttocks, large foul fatty stools, and symptoms of avitaminosis, first attracted attention.

Greater knowledge and experience have taught that there are all degrees of the disease which can be recognized. Early diagnosis and correct treatment have made the severe cases comparatively infrequent in this country.

DESCRIPTION

Two types must be considered in a description of celiac disease: The severe cases of long standing, due to neglect or unsatisfactory treatment, and the mild cases which may present only one or more of the usual symptoms. The former has been described so often that it is only necessary to recapitulate. It is rarely seen in a child under 1 year of age, for it takes time for the symptoms to be produced. There is a history of extreme irritability, profuse sweating, sleeplessness, marked asthenia, anorexia, rarely a voracious appetite, a prolonged diarrhea, continuous or intermittent, and occasionally vomiting and abdominal pain. None of the usual changes of diet seem to help. Examination shows marked pallor, a characteristic facies, and emaciation, best exemplified by the flattened pendulous buttocks. There is definite stunting in growth, a large abdomen, thin bones, and where the avitaminosis is great, glossitis, ecchymotic spots, and edema. The child lies quiet, whimpering, and cries when touched; he is unable to move the extremities because of a paresis of the parts. In some cases there is increased cardiac dullness.

The milder cases may arise so insidiously that there is no suspicion of their true nature. The most frequent symptoms calling attention to the possible existence of the disease are anorexia and diarrhea, and large stools, pale and foul, although in some cases there may be constipation. There is usually a history of failure to gain in weight, and growth is slow or entirely interrupted. The child may show no signs of unhappiness although inclined to be irritable. The abdomen is not enlarged, and there is absence of flattened buttocks. Emaciation is usually slight, and there are no definite symptoms of avitaminosis.

INCIDENCE

Celiac disease may begin at any age, often in the first months of life, but heretofore unrecognized in its early stages; symptoms of carbohydrate intolerance may appear even in the first weeks of life, i.e., frequent loose stools, and failure to gain in weight.

The disease is by no means as uncommon as was formerly believed, owing to the recognition of the milder cases. It would appear to occur more frequently among the poor and middle classes than among the well-to-do, and in this country is seen less frequently in hospitals than in private practice, which is contrary to the English experience.

It is likely to occur in several members of a family, in near or remote relatives.[11] Sauer[12] believes the disease may be transmitted, but I have never seen this nor am I familiar with other reports in the literature supporting this view.

COURSE

The course of the disease under correct treatment is very satisfactory; progress is regular and usually rapid, improvement sets in almost immediately, weight increases, the irritability and querulousness lessen, appetite improves, the stools become normal in appearance and less frequent, and after six to eight weeks the child acts normally and begins to grow in length. From the very beginning of the treatment there is no relapse from the disease itself. Relapses occur only as the result of an acute infection or a departure from a strict celiac diet. The tendency to relapse from infection diminishes as the celiac disease improves, but may occur from this cause until the disease is cured, after which there is no relapse from any cause.

Although all the active symptoms of the disease disappear early in the treatment, a strict diet must be maintained for at least a year and occasionally for as long as three years; failure to follow this rule may result in a relapse long after apparent cure.

DIAGNOSIS

Severe cases form a typical unforgettable picture which can hardly be mistaken for any other condition, although there is no individual symptom pathognomonic of the disease. In the milder cases anorexia and history of repeated attacks of diarrhea make the diagnosis probable, and the use of a strict carbohydrate-free diet, which I have termed a "celiac diet," will prove or disprove the diagnosis depending on the therapeutic response.

Substantiation of the diagnosis in either the mild or severe types may be aided by the presence of a low blood sugar curve[13] which is flat in the active stage and approaches normal during convalescence. Although characteristic of and usually found in celiac disease, it is not pathognomonic,[14] since the low blood sugar curve, one in which the rise does

not exceed 40 mg. per cent, is an inconstant phenomenon in about 5 per cent of normal individuals and is present in about 50 per cent of the cases of idiopathic steatorrhea.[15] It is also said to be found in marasmus, in any prolonged intestinal disturbance, and in cretinism.

There has been some work to show that the vitamin A absorption curve is low in celiac disease[16] but normal in some other types of steatorrhea. This may perhaps be of value in diagnosis.

Steatorrhea, although fairly characteristic of celiac disease, is not pathognomonic, for it is found in: congenital steatorrhea (fibrosis of pancreas),[17] tropical sprue,[16a] intestinal tuberculosis, excessive fat feeding, acholia,[18] severe diarrhea,[19] duodenal fistula,[20] pancreatic disease, and obstruction of the pancreatic duct.[21]

The avitaminosis may occur in any other disease where there is a lack of accessory food factors from any cause.

It is well known that infantilism occurs in many conditions, and although a striking and regular manifestation of severe celiac disease, it is in no sense pathognomonic unless it can be shown to be related to the intestinal disturbance.

Achylia is not found in celiac disease, and the blood picture is variable.

PROGNOSIS

The prognosis of celiac disease under the high protein banana diet is excellent. Of more than 200 patients seen in hospitals, consultation, and private practice, 134 consecutive patients were treated by me. The only therapy used was diet plus vitamin D and sometimes iron. One patient died of influenzal bronchopneumonia in the second week of treatment. One died of essential nephrosis, long after a cure had been effected. One, although recovered from the celiac condition, at 15 years of age is underweight and undersize, equaling a 10-year-old boy; he is scoliatic, with absent knee jerks, somewhat ataxic, and is believed to have suffered an attack of poliomyelitis. This is the only failure in the series, if it can be so considered. One proved to be a diabetic, probably a fibrosis of the pancreas. One, an adult, although generally well, is sensitive to carbohydrates and has an occasional loose stool. This is probably a case of sprue and is certainly benefited by injections of liver extract. The remainder are alive and well; seventeen cases are too recent to be of value in this analysis, although all of the patients are progressing satisfactorily. The eight patients for whom the diet was first used, after fifteen years are healthy, normal individuals. All are of normal height or above, five are of normal weight or above, three are underweight. All are on a full diet. There have been no relapses, and this small group can in no way be distinguished from any similar group in which celiac disease had never existed.

Among the remaining cases there have been no relapses so far as known.

In the entire series, of which forty-nine were males and sixty-six females, all are normal or above normal in height, eighty-six are normal or above normal in weight, nineteen (20 per cent) are below normal in weight. Of the underweights, 73 per cent are females.

TREATMENT

The treatment of celiac disease is one of diet alone, and this has held for the adult as well as the child. Failure to respond to the so-called celiac diet means that the patient has not celiac disease.

The correct treatment is exceedingly simple. A few principles must be borne in mind: first, no milk as such may be used; second, no sugar or starch in any form, excepting as it occurs in bananas and oranges and in protein milk or calcium caseinate milk or cottage cheese, may be used; third, protein may be used in any form as meat, egg white, gelatin, protein milk, calcium caseinate milk, cottage cheese.

This is the basic diet.

When the diagnosis is made or a suspicion of celiac disease exists the following diet is prescribed:

Breakfast.—Orange juice, cottage cheese, bananas, protein milk for children less than 2 years of age, and calcium caseinate milk for older children and adults, in any quantity desired by the patient.

Lunch.—Meat, liberal portion, preferably broiled or roasted, bananas, protein or calcium caseinate milk, and sugar-free gelatin.

Supper.—The same as breakfast; or egg white and bacon, may replace the cheese. Saccharin to be used for all sweetening.

Between Meals.—The permitted milk preparations and bananas may be used as desired.

Much Later.—Vegetables, except potato, and other fruits may be tried very carefully, one at a time. As a rule vegetables are not very well tolerated early in the treatment.

This diet, even in the face of apparent normality, should be continued for at least a year, when starch in the form of toast or cereal may be tried in addition, with the understanding that upon the reappearance of any symptom such as diarrhea, anorexia, or irritability it should be at once discontinued, to be tested again after three months.

If no ill results have followed by the end of three months, plain milk may be added with the same precautions and strictures.

If there have been no ill results at the end of another three months, then a full diet may be used and it will be found well tolerated. Sugar should be restricted in quantity for a long time.

During the course of the disease there is a variation in the tolerance for fats; some are more easily digested than others. Butter, as a rule, can be used early and freely, and sour cream is better tolerated than fresh cream; but cod-liver oil is not tolerated at all, although it has occasionally been reported as resulting in benefit. In my experience, egg yolk is frequently the cause of trouble.

The only vitamin required is vitamin D in concentrated, preferably dry form. This should be started after the diet is well initiated, early in the treatment.

The anemia is sometimes stubborn, and iron taken early in some form is advisable early.

Change of climate, massage, transfusion, etc., may be used, but are unnecessary, and hospitalization is necessary only when complications exist.

DISCUSSION

The value of banana in the treatment of celiac disease may depend upon one or more of the folllowing factors: First, it is rich in levulose. Mason and Sly[22] have shown that levulose or galactose can act differently from dextrose in the body, perhaps opening a new vista to the action of carbohydrates; however, the case upon which this observation was made was one of celiac disease, which may account for the better utilization of levulose, if not for galactose.

Mann[23] finds that levulose can be well utilized by hepatectomized animals for the formation of muscle glycogen, "although an apparently contrary opinion is expressed in that the tolerance for levulose is more often disturbed in clinical and experimental hepatic disorders than is that for glucose."

It has been found that sucrose and fructose, which make up a large part of bananas, raise the respiratory quotient to a greater extent than other sugars do, probably due to the large amount of lactic acid formed as the immediate intermediary product of these sugars.[24]

In healthy children, bananas as compared with glucose show a blood sugar curve only slightly higher, 9.1 mg. per cent; but in children suffering from celiac disease, bananas increase the blood sugar curve 50.2 mg. per cent and glucose only 22.9 mg. per cent.

The rise after equal amounts of levulose and dextrose is much less than the rise after an equal amount of banana.

It would appear, therefore, that the carbohydrate contained in banana is capable of raising the blood sugar to a normal height, which neither glucose nor levulose is able to do.[25]

In celiac disease dextrose produces a very flat curve; the curve obtained after the ingestion of a mixture of equal proportions of levulose and dextrose is similar to that found in normal children after the ingestion of dextrose.[26]

There also are certain enzymes in banana capable of converting starch into sugar.[27]

Kahn has said: "It is possible to convert the stool of a normal infant from an almost complete gram-negative to an almost complete gram-positive state by the use of 5 per cent of banana powder in the formula. The same effect was produced by 5 per cent of an equal amount of sucrose and fructose. A possible explanation is that fructose is the least

well absorbed of the monosaccharides and offers an exceedingly favorable medium for the growth of the *Micrococcus ovis* and the gram-positive anaerobic intestinal bacteria."[28]

In other fruits and vegetables there exists carbohydrate in some degree, the action of which in celiac disease is similar to that contained in banana. Many of these fruits and vegetables unfortunately are laxative in themselves, thereby limiting their use; apple alone of the common fruits seems to be an exception.

Unfortunately, the idea arose among many that bananas were specific in celiac disease and that it was only necessary to add them to any diet to obtain a good result; it was not realized that as long as other carbohydrates were being used the banana was valueless.

Celiac disease, tropical sprue and nontropical sprue are believed to be identical conditions by some, especially Dr. Hess Thaysen,[1] whose excellent monograph, "Non Tropical Sprue, a Study in Idiopathic Steatorrhoea," would seem to prove beyond doubt that tropical and nontropical sprue are identical diseases, the only difference being that the patients in the one instance were never in the tropics.

Consideration of the subject would be simplified if in the future the term tropical sprue were used to include both types of the disease, for I believe that a given case of nontropical sprue is either definitely tropical sprue or it is definitely celiac disease.

Thaysen believes that celiac disease is only tropical sprue occurring in early life. This viewpoint is not entirely acceptable as it is insufficiently supported by the available evidence, although when the etiology is understood it may prove to have been correct.

It is the marked similarity in symptomatology between tropical sprue and celiac disease which has created confusion; for the presence in both conditions of steatorrhea, a low blood sugar curve, infantilism, and avitaminosis, tend toward mistaken interpretation. Steatorrhea is common to both but in the case of celiac disease this is the result of the absence of available carbohydrate necessary for the metabolism of the fats.

In the case of tropical sprue, as has been so splendidly demonstrated by Rhoads[30] and his collaborators, steatorrhea is due to the absence or imperfect interaction of certain gastric intrinsic and extrinsic factors.

The presence of large fatty stools, together with the use of the term steatorrhea in this relation, has fostered the idea that the fats are at fault. Although it is true that the stools in celiac disease contain an excess of fat, the same patient on a fat-free diet may present an equally fatty stool; "the fats in this instance are believed to come from the epithelium of the intestinal wall and the intestinal bacteria."[31]

The steatorrhea in celiac disease is apparently connected with the carbohydrate metabolism; clinically it is known that the tolerance for fats improves as the tolerance for carbohydrate increases. In a given case, a minute amount of carbohydrate will produce a steatorrhea even on a low fat intake, while with a high carbohydrate intake in the form

of banana, the same case will not develop steatorrhea, even though a much larger amount of fat is ingested.

This can be shown by the simple test of putting the patient on a strict celiac diet, and when the symptoms are under control, if sugar, bread, cereal, cake, or even potato is added, the symptoms of the disease will return, to be again controlled by the omission of the offending carbohydrate from the diet.

Studies in metabolism have revealed an interdependence of carbohydrates and fats. The influence of carbohydrates in facilitating the combustion of fats is well known. It has been shown that the amount of fat which can be satisfactorily used by the organism holds a definite relation to the amount of carbohydrate introduced into the body, and the human organism appears to be incapable of oxidizing the common fatty acids unless a certain amount of carbohydrate or materials capable of forming glucose is burned simultaneously.[31]

It is now known that the fecal lipids may consist largely of fatty material secreted into the bowels rather than unabsorbed food lipids; and in the human subject on the exclusion of bile from the intestine, the fatty acids of the feces were found to equal or exceed the intake, and yet 65 to 75 per cent of the labeled ingested fats was absorbed.[32]

According to present day belief the fatty acids liberated by enzymic action in the small intestine are absorbed into the epithelial cells and then resynthesized to neutral fat.[33]

There can be no question that fats are poorly borne in celiac disease; but this depends chiefly upon the poor utilization of the carbohydrates, for from the beginning of treatment a certain amount of fat can be tolerated, an amount which increases rapidly with the improved utilization of the carbohydrates.

That the fats per se are not at fault in celiac disease is demonstrated by the use of protein milk, each quart of which contains 4 oz. of 20 per cent cream.

At the beginning of treatment I have used with excellent results, in this form, as much as 70 gm. of fat every twenty-four hours over an extended period. Only once was it necessary to avoid cream in making the protein milk. In this instance its replacement by an equal amount of butter was successful.

That the fats are of great importance in the celiac diet is well illustrated by the following report:

A girl 3¼ years of age, suffering from a severe case of the disease, was placed upon the ideal celiac diet, except that it was made as nearly fat-free as possible. With this diet she made a good symptomatic recovery. In nine months she gained 13¾ pounds but grew only ¾ of an inch. The fat was then returned to the diet, and during the following seven months she grew 3 inches and gained 7 pounds, and in the next eight months, another 3 inches, a rate five times as rapid as that of the fat-free period. In the next year there was a high normal gain of 3 inches, so that at 5¼ years of age her height was 42⅛ inches and her weight was 44¾ pounds, normal for the age.

This is in line with experimental work which has been done on rats by Mendel and others.[34]

Neither skimmed milk, nor lactic acid nor buttermilk can be successfully used, although in a few cases fermented milks have proved satisfactory late in the treatment.

The good results in celiac disease of an exclusive high protein diet may be accounted for by the conversion of approximately one-half the protein into carbohydrate, thus supplying the body's need for carbohydrate.

According to many, especially Parsons,[2] many cases of celiac disease show low calcium levels, often low phosphorus levels, thin brittle bones, and osteoporosis; tetany is common. Parsons has gone into this phase of the subject thoroughly and his work is detailed and authoritative; consequently, it has been a surprise that among all the cases of celiac disease which I have seen, the only clinical manifestation of tetany has been perhaps the abdominal colic. The cases are usually flaccid, and perhaps fail to show the usual symptoms because they are fed fat from the beginning and receive vitamin D early.

It has been found[35] that there is a marked reduction in the production of glycero- and hexosediphosphatase in the intestines of all patients with celiac disease, a finding which may prove to be of importance in its pathogenesis.

Herter's findings that there is an absence of the colon group and that the bacteria in the stools of patients with celiac disease are predominently gram-positive aciduric organisms which retain their infantile characteristics, particularly B. bifidus and B. infantilis, whose numbers rise and fall with the fluctuations in the course of the disease, have not been accepted as an explanation for its etiology, although Brown[36] and his collaborators "in its principal point have confirmed Herter's work."

Compatible with the theory of a bacterial background for the etiology of celiac disease is the experience that in treatment including a rigid celiac diet, relapse may occur from the addition of carbohydrate up to a certain time, after which relapses cannot be induced by any measure. The whole proceeding gives the impression that some organism requiring carbohydrate for its propagation continues to grow until deprived of its proper medium for a sufficient period, when it disappears from the intestinal tract, not to appear even though the carbohydrate which previously continued the disease may be fed in large amount. Experimentally[37] it has been shown that upon the addition of starch to the medium, bacteria can produce enterotoxic substances and can restore these substances after their exhaustion, when starch is again added. Although lack of evidence makes a bacterial etiology highly speculative, the idea is certainly worth continued consideration.

From this conflicting mass of evidence and theory there arise certain facts which have the appearance of truths and which can be used as a basis for further investigation and treatment.

CONCLUSIONS

Celiac disease is due primarily to a carbohydrate intolerance. It can be cured by a celiac diet. The differential diagnosis between celiac disease and the other steatorrheas can be made by the response to the celiac diet. The prognosis under correct treatment is excellent as to life and immediate and future health.

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Special Article

THE NATIONAL HEALTH CONFERENCE

How the Conference Came to Be Called.—At the time the Social Security Act of 1935 was being prepared and discussed, an attempt was made to include a number of "health" provisions. So much controversy developed about the question of health insurance and other matters, and there were so few factual data upon which to inaugurate legislation, that the subject was largely omitted from the provisions of the Act. Certain sections relating to the "Public Health Service" and "Maternal and Child Welfare" were, however, included.

In August, 1935, following the passage of the Act, President Roosevelt appointed an "Interdepartmental Committee to Coordinate Health and Welfare Activities," consisting of Assistant Secretaries of four governmental departments (Treasury, Interior, Labor and Agriculture) and the Chairman of the Social Security Board, in order that the full benefits of the various federal programs under the provision of the Act might be carried on with minimum delay and maximum effectiveness.

This Interdepartmental Committee in turn appointed a "Technical Committee on Medical Care" to study the subject and formulate a program. The Technical Committee consists of Dr. Martha Eliot of the Children's Bureau, Dr. Falk of the Social Security Board and Drs. Mountin, Perrott, and Waller of the United States Public Health Service. The report and national health program recommended by the Technical Committee to the Interdepartmental Committee was presented to the President on February 14, 1938. At the suggestion of the President a "National Conference on Health and Medical Care" was called by the Interdepartmental Committee in Washington on July 18, 19, and 20, at which the recommendations of the Technical Committee were presented for discussion.

Invitations to attend the Conference were extended through the Chairman of the Interdepartmental Committee, Miss Josephine Roche, to men and women from the medical profession, from agencies actively interested in health and medical services, and from labor, agriculture, and other groups of citizens.

The purposes of the Conferences as stated by the Chairman were:

(1) To present and discuss the needs of the people of this country for preventive and curative service in illness and for the reduction of the economic burdens caused by illness, as revealed by governmental and other studies.

(2) To discuss steps which may be taken to meet these needs, as proposed by representatives of the government and by members of the conference.

It was distinctly understood and clearly stated that it was not the purpose of the Conference to take action on the recommendations as presented by the Technical Committee. Members of the Conference, however, were invited to present any program they had in mind.

A mimeographed report on "The Need for a National Health Program" was made available some time ago and has had a limited discussion in medical journals. Part of the information forming the basis of the report was obtained from the "National Health Survey" made by the United States Public Health Service in the winter of 1935-36, in which, for example, three-quarters of a million families in 84 urban centers of different sizes were canvassed and detailed information was obtained as to income, illnesses, and the extent of medical care.

The program recommended by the Technical Committee, in the form of five resolutions, was not available, as a whole at least, to the members of the Conference before the time of the meeting. Certain parts were sent a few days before the meeting to certain members selected for their interest in some particular phase, with the request that they take part in the discussion.

Composition of the Conference.—The nature of the conference is well pictured by a glance at its composition. In all there were 171 members, of whom about 80 took part in the discussions. In addition there were almost an equal number admitted as "observers" who were seated in the balcony, but took no part in the proceedings. A break-up of the membership shows the broad character of the interests represented. Somewhat less than a third were physicians. Resolving this group into parts, 6 were representatives of the American Medical Association although it was stated that in the entire membership there were 10 members of the House of Delegates present. There were 10 representatives of special fields, as tuberculosis, mental hygiene, obstetrics, etc. Nine were heads of city and state departments of health, and in addition several represented voluntary health organizations. About 10 belonged to specific hospital and industrial groups. A few represented organizations such as the Red Cross and College of Surgeons. Some 7 or 8 represented no particular category or organization, but were present as individuals. Several of these were members of the "liberal" group which has banded itself together loosely as the "Committee of Physicians." Many as a matter of fact represented several phases of interest or activities.

Over two-thirds of the members were "lay" and these may again be divided up into several groups. There was a large professional group made up of social workers, nurses, dentists, hospital executives, etc., who are working directly in the field of health. A smaller group was made up of board members, community workers, officers of women's organizations, and the like. A third large division was made up of representatives of what was referred to many times as the "consumer," viz., public welfare agencies, labor, and agriculture. There were over twenty representatives of labor, including the President of the A. F. L. and the Chief Counsel of both the A. F. L. and the C. I. O. For the purpose of the conference the labor group stood closely together. Some 10 representatives of agriculture and farm organizations were included. Nearly 15 journalists including members of the editorial staff of such magazines as *Time, Good Housekeeping, Survey, Liberty,* and *New Republic,* formed another distinct group.

That the membership was carefully picked to represent all phases of the question of medical care there was not the slightest doubt. The intermingling of the "technical" group with the "consumer" group marked a new phase of health conferences. The intermingling was further marked by seating the members alphabetically rather than by group interest or personal choice.

Program

The first day was given over to introductory remarks and scheduled discussions. On the second day there were three sessions at which the five recommendations for a program, which are discussed below, were presented. The third day was entirely given over to discussion by the members of the Conference, although considerable open discussion took place on both the first and second days. Members of the Interdepartmental Committee, Messrs. Altmeyer, Wilson and Chapman, presided at the various sessions.

Session I, Monday Morning, July 18, 1938.—The conference was opened by Miss Roche, who presented a message from the President which ended with the statement, "I hope that at the National Health Conference a chart for continuing concerted action will begin to take form."

Miss Roche then welcomed the members and began the theme of the first day's session, which was the "Need for Medical Care." The viewpoint of the present government was summed up in the remark, "We have established the principle that certain insecurities which individuals alone are powerless to withstand must be met through public action, that human conservation is an obligation of government." She then in a general way outlined the Committee's findings on needs. Stress was placed on economic differences. Among families on relief acute illness is 47% more prevalent and chronic illness 87% more prevalent than among families with incomes of $3000 or over. "No physician's care is received in 30 per cent of serious disabling illnesses among relief families, and in 28 per cent of such families just above the relief level." ". . . the death rate among infants in families with incomes of $500 was more than five times the death rate among families with incomes of $3000 or more." "Half of the two million babies born each year—a million babies—are born to families either on relief or with less than $1000 annual income." "Fifty million Americans are in families receiving less than $1000 income a year." "On the average day of the year, four million or more persons in the United States are disabled by illness." "The total cost of illness and premature death in this country is approximately ten billion dollars a year. This estimate includes only those factors which can be expressed in dollar values—the cost of health service and medical care, the loss of wages through unemployment resulting from disability and the loss of potential future earnings through death." The speaker pointed out that everything proposed could not be put into effect at once and that time would be required to put a full program into operation.

Miss Katherine Lenroot, Chief of the Children's Bureau of the Department of Labor, then spoke on the subject of "Health Needs of Mothers and Children," discussing the problems of income and food for the family, the question of the infant mortality rate, the lack of medical care for the mothers and children in many areas, the lack of hospital facilities and medical care for children. "A total loss of maternal and early infant life amounting to 160,000 a year, at least half of which is preventable." Forty of 49 State Health Officers declared that facilities for maternal care in their states are definitely inadequate. ". . . as in meeting mass disaster, the needs of mothers and children require that they be among the first to be cared for."

Dr. Thomas Parran, Surgeon General of the United States Public Health Service, concluded the brief program of the first session. He spoke of the necessity for increased emphasis upon the prevention of disease and the vital function of research. "It is my firm belief that this Conference marks the ridge of the hill between the old indifference to health as a matter of national concern and a new understanding that health is the first and most appropriate object for national action." "The significance of this meeting does not lie in the fact that it involves contemplation and discussion of health needs . . . discussion is requested of you as a preliminary to practical action by responsible government agencies." "It is not unlikely that public health may be the next great social issue in this country." "You are here to suggest the best, most practical and most profitable ways and means of putting medical science to work." ". . . we should not continue to think in terms of the separateness of public, private and voluntary efforts or of the separateness of preventive or curative efforts to reduce death and disease . . . all are parts of the same entity."

The inability for economists to solve our problems was pointed out and that medicine and public health should lead economics rather than follow it, as our proved ability to prevent disease exceeds greatly our proved ability to control other causes of poverty. "Medical education and practice must keep pace with advances in science and with changing social concepts."

"This Conference may reveal differences of opinion concerning the role of the federal government in putting medical knowledge to work for the benefit of all citizens. There can be no disagreement, however, with the principle that the federal government must increasingly assume leadership in the study of those great causes of disease and death before which we are now helpless." The coordination of investigative efforts and aid to scientific institutions were cited as examples of this government leadership.

Second Session. Monday Afternoon.—The second session started with a group of seven scheduled discussions. Dr. Irvin Abell, President of the American Medical Association, was the first speaker, and his address covered in general the same grounds as his address at San Francisco in June, which has been published in the *Journal of the American Medical Association.* He spoke in general of the work of the A. M. A.; the necessity of a plan under medical control. He felt it was impossible to isolate medical care from other unfulfilled needs, as food, clothing and housing. Dr. Abell stated that there could be little disagreement on certain fundamental objectives in regard to medical care, which were the provision of good medical care for all the people, the development of public health problems, and an improvement in the distribution of medical services and hospital facilities by geographic and economic division.

He was followed by Dorothy Kahn, Director of the Philadelphia County Relief Board, who spoke of the problem in obtaining good medical service for families on relief. The speaker felt it was difficult to obtain an idea of medical needs by a survey, but that when medical relief was given it brought out the needs.

The next two speakers, William Green, President of the A. F. L., and Dorothy J. Bellanca, Vice President of the Amalgamated Clothing Workers of America, discussed the problem in a broad way calling attention to the social and economic disintegration that results from sickness not only to the bread winner but to the children. The expansion of public health and maternal and child welfare services, the use of government funds to provide medical care for the needy, and the application of the insurance principle were urged by "labor." Mr. Green demanded compulsory insurance under government supervision for the low income group (under $3000) which he stated made up 87 per cent of the population even in the best times.

Next, two "Farm" representatives spoke, Benjamin Kilgore, Executive Secretary of the Kentucky Farm Bureau Federation, and Mrs. H. W. Ahart, President, Associated Women, American Farm Bureau. Both stated the farm people wanted better medical service and hospitals—medical service comparable to that obtainable in the urban districts which at the present time was not available for the farmer. Resolutions of the American Farm Bureau Federation were presented calling for the establishment of rural hospitals where they are needed and could be maintained on a good professional and financial standard, acknowledging the advantages of health insurance and pledging itself to work for such laws, and third the extension of all forms of preventive medicine throughout the country. Mrs. Ahart stated they had no quarrel with the American Medical Association but insisted the medical fraternity had a grave responsibility to the public and asked for greater cooperation between the medical profession and the lay public. "The demand for health insurance and for adequate medical care for our entire population, both urban and rural, is a force that must be recognized, despite any objections expressed by individuals within the medical profession."

The last scheduled speaker was Dr. Hugh Cabot. After referring to the rising tide of the "consumer," he stated he thought the fact of need was quite beyond discussion. He felt that further surveys to determine if needs existed were superfluous, and, referring to the survey now being carried on by the American Medical As-

sociation, that physicians were poorly qualified to carry out a survey. He felt further discussion of the need of improvement in medical care was futile and our attention should be turned to methods of improving care.

Several members were then called upon to speak whose remarks are included under the heading "Discussion" below.

Sessions III, IV and V. Tuesday, July 19.—At the three sessions on Tuesday, the five programs and recommendations of the Technical Committee were presented. "Maternal and Child Health" and "Public Health Service" in the morning, "Medical Care for the Medically Indigent" and "Hospitals" in the afternoon, and at the evening session (a) "A General Program for Medical Care" and (b) "Insurance against Loss of Wages During Sickness." All of the presentations followed the general plan of a brief summary of the needs, followed by the recommendations of the Committee, and ending with a brief discussion of plans and estimates of cost.

Program and Recommendations for Maternal and Child Health. Presented by Dr. Martha Elliot, Assistant Chief of the Children's Bureau.

This was presented first as the Committee was of the opinion that in any plan for a national health program primary consideration must be given to the subject of maternal and child health.

Attention was called to the high maternal death rate in the United States, to the 75,000 stillbirths each year, and to the death of 70,000 infants in the first month of life. Over 1,100,000 births occur in families on relief or with an income of less than $1,000 a year. Physicians estimate that from one-half to two-thirds of the maternal deaths are preventable, that the stillbirth rate can be reduced by two-fifths, and that the newborn infant deaths can be reduced by one-third to one-half. The total extent of dental defects, rheumatic disease, visual defects, crippling, etc., among children was pointed out, and the place of infectious diseases as a cause of illness and death in childhood. The need for consultation services in obstetrics and pediatrics was mentioned, and the national character of the problem with its economic and geographic differences was stressed. For example, 11 states in the Southeast, caring for 25 per cent of the children, receive only 12 per cent of the national income, while 12 states in the Northeast, caring for 29 per cent of the nation's children, receive 41 per cent of the income.

The Committee recommended expansion of the existing Federal-State cooperative program for Maternal and Child Welfare services under Title V of the Social Security Act, over and above the $3,800,000 now available. The program should provide facilities for (a) medical and nursing care for mothers throughout maternity, and (b) health supervision and medical care for children. The plan for extension under (a) called for the medical care of mothers and newborn infants, including delivery, by qualified local physicians assisted by nurses, facilities for expert diagnosis and consultation in centers and in the home, and hospital care when necessary for medical or economic reasons; under (b) health supervision and medical care by local physicians, the aid of specialized consultants and hospitalization when necessary. Increased opportunities for post graduate training of professional personnel were considered as essential in carrying out the program.

It was estimated that the cost to the federal, state and local governments of a program for the maternity and newborn services for families with an income level of $1000 or under, would be $95,000,000 a year, with a maximum federal participation of approximately one-half of this amount. It was recommended that for the first year the present federal appropriation should be increased by $4,500,000, and that the annual appropriation be gradually increased until it reached $35,000,000 by five years, and the total amount in not less than 10 years.

It was estimated that medical care for the 13,000,000 children under 15 years of age in the medically indigent group would cost $130,000,000 a year. Part of this would be carried by the provisions of Recommendations II and III ("Hospitals" and "Medical Care for the Indigent"). The Committee recommended that a sum beginning with $3,000,000 a year and increasing gradually to $30,000,000 by the tenth year should be provided for the medical care of children by the Children's Bureau under Title V, part 1, of the Social Security Act.

Under Title V, part 2, of the Act, an additional appropriation over and above the $2,850,000 now available was recommended for services for crippled children.

The Committee felt that the part played by the federal government in the early years, when the program was developing, should be relatively large, supplementing present expenditures by the state and local communities. In apportioning money to states such factors as the ability of the state to provide support, and the need for maternal and child health care as shown by the mortality and morbidity rates, should be taken into consideration.

In recapitulation the program recommended increased appropriations above amounts now available for expenditure under Title V of the Social Security Act, for Federal grants-in-aid to the states of $9,500,000 the first year, increasing gradually to a total of $82,500,000 by the tenth year.

Program for Public Health Services. Presented by Dr. Clifford E. Waller, United States Public Health Service.

The need for an increase in full time health administration, particularly in rural areas and smaller cities, and in inadequate state organizations was first pointed out, and the work of the United States Public Health Service under the provisions of the Social Security Act in the last few years.

Certain problems were discussed specifically. Tuberculosis with its spread from active cases. Venereal disease, in which early and adequate treatment is the only possible method of cutting down the incidence. Increased laboratory facilities and better treatment facilities are urgently needed. Some 60,000 cases of congenital syphilis occur yearly. By the development of serum treatment for pneumonia, which implies increased diagnostic laboratory facilities, the gross death rate of 150,000 annually could be reduced 25 per cent. Only eight states have active programs for typing and distribution of serum. Cancer with its high death rate is an active program in only seven states. Malaria control in the southern states is essential. Institutional care for the mentally ill is but part of the mental hygiene problem. Preventive facilities and services should be extended. Laboratory and field research is needed in the field of industrial hygiene as 15,000,000 people are engaged in productive occupations.

The Committee recommended the expansion of the existing Federal-State Cooperative Program under Title VI (Public Health Work) of the Social Security Act. Federal participation in state and local health services to be extended through increased authorization for grants-in-aid to the states.

Primary consideration under the program would be given to the development of local health organizations on a full time basis. The tuberculosis campaign would be carried on through case finding and isolation of active cases. Venereal disease would be attacked along the lines now being carried out. The pneumonia campaign would be to increase laboratory facilities and the free distribution of serum for the medically indigent. For cancer the setting up of diagnostic and treatment centers is required. An extension of the work of present hospitals or new centers might both be used. An adequate staff and therapeutic apparatus, as radium and deep x-ray therapy, are essential. The program for mental hygiene involves assistance to existing institutions and improved diagnostic and treatment facilities. Mental hygiene centers for the early preventive treatment of maladjustments must

be provided. An industrial hygiene unit should be developed in every state with adequate laboratory and field workers. Prior to 1936 only 3 states and 1 city had programs for industrial health. Since 1936, under Title VI of the Social Security Act, units have been organized by federal assistance in 21 additional state departments of health. Departments should be developed in all states.

The total estimated maximum annual cost for all services would be $200,000,000. This includes federal, state and local expenditures combined.

Public health organization	$23,000,000
Tuberculosis	43,000,000
Venereal disease	47,000,000
Pneumonia	22,000,000
Cancer	25,000,000
Malaria	10,000,000
Mental Hygiene	10,000,000
Industrial Hygiene	20,000,000
	$200,000,000

It is not assumed that all items would remain at these maximum figures. It is considered proper that the federal government should contribute half of the amount. The Committee recommends that the initial federal appropriation should be $10,000,000 the first year, with a gradual annual increase to the maximum of $100,000,000 by the seventh year.

Hospital Facilities. Presented by Joseph W. Mountin of the United States Public Health Service.

The extent and control of existing hospitals was discussed. General hospitals by number are one-half nonprofit organizations, one-third proprietary, and 15 per cent operated by state and local governments. By beds, 27 per cent are governmental, 62 per cent nonprofit, and about 11 per cent are proprietarily owned. Fees collected from patients form 70 per cent of the income of nonprofit hospitals and 6 per cent of the income comes from endowment. Over 40 per cent of the counties in the United States do not contain a registered general hospital—the population of these counties amounts to 17,000,000. The ratio of beds per 1000 population exceeds 5.2 in 23 large cities of 200,000 or more inhabitants.

Hospital facilities exceed 4.7 per 1000 of population in 25 per cent of the states. Beyond the metropolitan counties 3.1 beds are found in 25 per cent of the states. On combining location with ownership, general hospital service is not available to a large segment of the population either through faulty location or inability to purchase care. Average occupancy is about 70 per cent of capacity, but in hospitals depending on revenue from patients it is 50 per cent. In tuberculosis sanitaria the bed occupancy amounts to 92 per cent of capacity where less than 10 per cent of the cost is paid by patients, and falls to 67 per cent when the revenue from patients amounts to 90 per cent or more. State and local governments have a practical monopoly (92 per cent) of institutions for the insane. Out patient services are most important in caring for the medically indigent. Each city over 250,000 has one or more such department, while only 2 per cent of cities under 10,000 have such resources. About half of the cities of 50,000 have outpatient services.

The Committee recommended federal grants-in-aid for the construction of needed hospitals and related facilities, and special grants on a diminishing basis toward defraying the operating costs of these new institutions in the first three years of their existence.

To bring all state averages for general hospitals up to 4.5 would require 180,000 additional beds. Some should be added to existing units and some would call for

new units. The Committee estimates a need for 500 new hospitals, in areas largely rural in character, of a 30 to 60 bed capacity. There should be 2 sanitaria beds for tuberculosis for each death. This would call for an addition of 50,000 beds. Many of these should be incorporated into existing institutions, but in several states new institutions should be established. Mental institutions call for a capacity of 4.8 beds for 1000 population. This would call for 130,000 additional beds.

The estimated cost of such construction would be

General Hospitals	$ 630,000,000
Tuberculosis Hospitals	150,000,000
Mental Hospitals	325,000,000
	$1,105,000,000

For the construction program the Committee recommends federal government grants-in-aid equivalent to 50 per cent of the cost, or $552,250,000. Temporary maintenance grants over a period of three years were calculated at a total of $177,000,000. This construction program would extend through several years.

Medical Care for the Medically Needy. Presented by George St. John Perrot of the United States Public Health Service.

The formulation of a national health program implies acceptance of the principle that the maintenance of the health of its citizens is a responsibility of government. Government has assumed responsibility for the provisions of preventive health services on a community-wide basis, but wide variations exist throughout the country in the practical application of this policy. A more serious situation arises from the inertia of governmental bodies in the field of medical care of the needy sick. With some important exceptions medical care is "an economic commodity" purchased and paid for directly by the individual who needs it. The fact that it is chiefly a professional service does not alter the basic fact.

In the United States there are today probably 40,000,000 persons—almost one-third of the population—living in families with an income of less than $800. This sum supports the family at an emergency level. In this group are 11,000,000 in families on work relief, 6,000,000 in families on general relief and 3,000,000 wards of the government under the Social Security Act (dependent children, old age, dependent blind). This group of 20,000,000 is dependent on government for food, shelter and medical care. In the emergency of sickness 20 million more in the marginal income class become dependent on public aid for medical care.

In the 40 million there will be 20 million cases annually of disabling illness of which 8 million will be of at least a week's duration. Two million of the disabling illnesses will receive no medical care and the 6 million medically attended cases will include 2 million patients in general hospitals. It will include 250,000 cases of pneumonia, 190,000 cases of appendicitis, 425,000 cases of tonsillitis, etc.

There is an uneven distribution of our resources for the maintenance of health. A large population of the medically needy are found in small cities and rural areas in which facilities for care are limited.

The medical needs of this low income group exceed those of families at higher economic levels as demonstrated by numerous surveys. Among children in relief families the annual days of disability was 17 per cent higher per capita than the average for families of higher economic levels.

One in every 20 family heads in the relief population was unable to work on account of illness, contrasted with 1 in 250 in families with an income of $3000 or more. The tuberculosis case rate is 10 times as high under similar income conditions.

Despite this greater need, studies "before depression" showed well-to-do sick persons received 3 times as much medical service as the poor.

In 1935 the survey of the Public Health Service showed hospitalization was about the same for the rich and poor in the large cities, but the proportion of poor hospitalized in small cities and rural areas declined rapidly. In discussing the present financial basis of public medical care it was stated that in 1935 governmental expenditures for health and medical care amounted to one-sixth of the total medical bill for that year, or $520,000,000. After deducting expenditures for patients in federal hospitals, public health services, etc., a sum remains of roughly $130,000,000 which was spent for tax supported medical care for the needy. It is estimated that the cost of essential medical services at the emergency level for the medical needy would amount to about $400,000,000 annually.

The Committee recommended Federal grants-in-aid to the states toward the costs of a medical care program for recipients of public assistance and other medically needy persons.

Two broad groups of the population would be included (a) those for whom government has already accepted some responsibility through public assistance, and (b) those who, able to obtain food, clothing and shelter, are unable to obtain necessary medical care.

The program would be developed around existing preventive health services. It would provide minimum essential needs, including medical and surgical care, hospitalization, care of the tuberculous and mentally ill, bedside nursing and emergency dental care. It would extend to 40,000,000 persons in families under the $800 income level group. The total figure is based on an estimate of $10 per person. The proposed federal contribution might amount on the average to 50 per cent, or $200,000,000 annually. It is suggested that a start should be made in the first year of $50,000,000 increasing annually to the maximal expenditure at 10 years. This sum is over and above the recommendation for public health services.

A. *"A General Program of Medical Care."* B. *"Insurance Against Loss of Wages During Sickness."* Presented by Dr. I. S. Falk, Social Security Board.

Medical facilities are of no direct benefit to persons who do not use them. The most important barrier between individuals or institutions equipped to serve the sick, and the millions of people in need of this service is an economic wall. The cost of medical care must be brought within the means of the public.

The total expenditures in 1929 for all kinds of health and sickness services were about $3,700,000,000, of which patients paid 79 per cent, government 14 per cent and philanthropy and industry the remaining 7 per cent. In 1936 the total expenditures had declined to $3,200,000,000 of which patients paid 80 per cent and government 16 per cent.

Medical services to be effective must be geared to need. All studies and surveys show sickness is more prevalent among people of the low income groups. The well-to-do do not receive too much care—the poor receive too little. The large majority of people receive medical care not according to their needs but according to their income.

The average family with an income up to $5000 spends 4 to 5 per cent of the income for medical care. Average figures do not give a realistic picture, as the need by a specific family is uneven and unpredictable. Serious illness may be a catastrophe to the family budget. The burden is not due to the average expenditure, but to the unevenness. The savings of a lifetime are at times wiped out and the whole level of family life and security lowered by the economic loss of sickness. The adjustment of fees operates in only a limited way.

Adequate medical care purchased on an individual basis is estimated to cost $76 per year per person. On a group basis it can be purchased for $25 a year. Expenditures on this basis would mean doubling the amount now spent by families in the $1000 level, adding one-fifth to the $2000 level (60-80 per cent of the nation).

Families with incomes of $3000 or more spend more than $100 per year. "If medical care is to be made available to all families with small or modest incomes at costs they can afford, the costs must be spread among groups of people over periods of time."

The inadequate income of physicians deserves careful consideration. In 1929 for every physician who earned $10,000 there were two who earned less than $2,500. Since 1929 the economic status of doctors has become worse. While doctors are only partially occupied, millions of people in need of service do not receive it. Every sound arrangement to reduce the burdens created by sickness costs operates to increase and stabilize the incomes of those who furnish the services.

Voluntary insurance efforts, in the opinion of the Committee, is not the answer to the nation's needs. Many of the devices practiced to meet the burdens and distribute the costs, as organized charity, sliding scale of medical fees and commercial insurance, have long been in use and are inadequate to meet the needs.

Group payment in various forms has become more important, especially group hospitalization; while commendable, the proof of their value lies in their actual accomplishment. Voluntary sickness insurance, with or without subsidy, may be important as a method of experimentation, but it has nowhere shown the possibility of reaching more than a small fraction of those who need its protection.

The Committee recommended federal grants-in-aid to the states toward the costs of a more general medical program.

The wide variations in existing personnel, institutions, and economic conditions require that a national program must be flexible and adopted to the diverse conditions existing in different parts of the country. Hence effective operating programs should be designed and administered on a statewide basis. The role of the federal government should be principally to give financial and technical aid to the development of state programs.

There are two methods of expanding public health services. By one the government can make particular kinds of services available, by the other a general program can be developed. The second has fewer drawbacks of an administrative nature and is not complicated by economic groups. A general program would cost about $2,750,000,000. New tax funds for public medical services would not represent a new kind of expenditure, as most of these sums are now being spent from private funds. A general program can be financed through insurance contributions. It might be limited to specified income levels. A general program should include the medically indigent, through maintenance by public funds, combined with the insured groups.

A choice between public medical services (tax supported) and health insurance involves many considerations. It may be best, according to type of the population of a given area, to develop both methods. This is a choice to be made by the states rather than the federal government. Federal grants-in-aid should within reasonable limits be available whatever procedure or method the states decide to follow. The eventual federal support would amount to between one-fifth and one-third of the $2,600,000,000 overall cost.

B. *Insurance Against Loss of Wages by Sickness.*—

There are probably 7 to 10 days of disability per person a year among the gainfully employed, with a range of from 3 to 4 days up to 15 or more a year per person. The total wage loss by disability in 1929 amounted to nearly two billion dollars. The average loss of time is relatively unimportant, but the incidence is uneven, extending up to a year, or permanent disability in many cases.

Under the present Social Security laws workers are assured of partial income when unemployed, and most are protected by workingmen's compensation from accident or injury arising from employment. There is no protection from non-industrial accident or sickness, except in a very few instances where there is voluntary insurance.

The Committee recommended federal action toward the development of programs of disability compensation.

Two coordinated systems would probably be better than a single insurance system. A system for temporary disability is best patterned after unemployment compensation. For permanent disability the system should be patterned after old age retirement. The first would cost approximately 1 per cent of wages, the second 0.1 to 0.2 per cent at the start with a gradually increasing cost to 1 to 2 per cent of wages in 20 years.

A disability program is not primarily part of a medical care program, but there are important interrelationships.

Discussion

Nearly 80 members of the Conference took part in the discussion. There was, however, very little specific discussion of the recommendations, nor was there any continuity to the discussion. It was obvious that most members who spoke came prepared to say some specific thing, and most frequently read from a prepared manuscript. This was presented whenever the member got the chance to take the floor. Thus a member discussed "insurance" before the insurance report had been presented Tuesday night. It has seemed best to present the discussion by groups and topics, therefore, rather than the order in which it came. Many members had the opportunity to speak Tuesday and the entire sixth and seventh sessions on Wednesday were given over to the members of the Conference.

Discussion by Medical Members.—Unfortunately a certain element of discord and personal feeling entered into the discussion by the physicians, which was "news" and hence featured in the newspapers, and which gave a somewhat false impression of the attitude of the medical members of the Conference as a whole.

After Dr. Abell and Dr. Cabot had spoken on the scheduled program of the second session as noted above, Dr. West, Secretary of the American Medical Association, took the floor on Monday afternoon and pitched into Dr. Cabot whose remarks he considered as a criticism of the American Medical Association. He then continued with a defensive discussion of the American Medical Association and the medical profession, which was a tactical error, as it opened the way for future discussion on this point. It gave a number of speakers the opportunity to attack the American Medical Association while praising the medical profession. To quote Mr. Lee Pressman, Counsel for the C. I. O.: "I do not criticize the individual doctors. I direct my attack specifically at the upper hierarchy of these medical associations that simply refuse to give adequate health to the people of this country." This is not quoted in support of Mr. Pressman's views but to illustrate the attitude taken by a member who spoke. There was no disagreement among the physicians present on Monday night, no matter what they represented or what their personal feelings or interests might be, that the medical profession as "organized medicine" had made a bad impression. The situation was so obvious that at his request Dr. Abell of the A. M. A. was given the floor the first thing on Tuesday morning and made some excellent conciliatory remarks, expressing the intention of organized medicine to cooperate. On Tuesday and Wednesday a number of physicians spoke in a general way, including Drs. Kerr, Peters, Veeder, Myers, Osgood, Hamilton, Grulee and Baehr. In general all expressed the attitude that they recognized medical needs were not being adequately met at the present time due to changing conditions,

the increase in the load of the medically indigent, and the rapid technical development of medical science with its corresponding increase in the cost of good medical care. The importance of providing for the maintenance and development of the highest medical standards in any program was stressed in one way or another by all. Dr. Osgood spoke of the necessity of independence of action of physicians as is dictated by their consciences. He threw out the suggestion of the possibility of a National Health Council, without executive power, to act in an advisory capacity in matters of health. The importance of medical education and training in any program was stressed by several. Dr. Alice Hamilton, who was called upon impromptu, gave one of the finest talks at the Conference. She stated while in some particulars the figures presented might be wrong, the aggregate picture was correct. Her impressions of the Conference were first of the very great need and secondly of a "body of people, the physicians, who have striven hard to meet the need, but who are suddenly faced with an increased demand which they themselves cannot meet." The "federal government is not an invading hostile power . . . it is ourselves—ourselves organized." She felt there would be certain losses in this new approach to the medical problem, but that every advance has been accompanied by the loss of something precious. She felt we must go forward and meet this new need and did not agree with those who think the need is temporary.

Dr. Fishbein, Editor of the *Journal of the American Medical Association*, spoke Wednesday morning and his remarks were widely quoted in the lay press which was playing up opposition to the program by the American Medical Association. Dr. Fishbein did not attack the program from the standpoint of socialized medicine, but rather that it was based on a temporary need and that he considered other needs as more important. "The fundamental needs of mankind are food, fuel, clothing, shelter and a job, and medical care and dental care must always be subservient to those main human needs." "Let us concern ourselves with that question of food, fuel, clothing, shelter and a job with adequate wages." The importance of these factors was denied by no one and was brought out as related to health several times in the Conference; the Conference, however, was called to discuss a program for medical care not basic economic problems.

Dr. George Baehr, Chairman, Committee on Public Relations of the New York Academy of Medicine, was the last medical speaker. He stated he spoke "as the average American physician who has been stood up before you throughout this Conference and buffeted about only to be stood up again by the next speaker in time to receive the next blow." "I feel that the medical profession has, partly because of the manner in which it has presented its case, left you with a wrong impression. The average American physician . . . is deeply in sympathy with improving the adequacy of medical care and is ready to agree with you as far as you wish to go, that medical care in many fields of medical activity is not adequate." ". . . you should be sure that we are really making progress forward and not backward." He spoke of how private enterprise had pointed the way to government in public health and considered some of the needs due to the failure of government support, and said that the responsibility must be laid at the door of government, not of the medical profession. He spoke of the vast number of communities served by political appointees. ". . . you are responsible for keeping in office the political administrations which are responsible for this, and therefore to lay these evils at the door of American medicine, to make a scapegoat of the medical profession and not to acknowledge your own responsibility humbly and join with us in making such progress as can be made, is entirely wrong."

Discussion by Labor.—One of the most interesting parts of the Conference was the discussion of the labor representatives. We have referred to the two scheduled discussions in the second session. Several of the union executives presented detailed

medical programs for their groups, which were of significance only as it showed they were thinking of and considering a health program in detail. Several of the speakers dramatically described the conditions of medical care under which the workers were existing. The demand for better medical care was clear and distinct, and the point was made that regardless of what the medical profession thought, they were not satisfied with the medical services available to them, and accused the organized medical profession of blocking progress toward better medical care. Some labor members stated they did not want insurance under state control, as recommended by the technical committee, but would only be satisfied with a federal controlled system. There was some difference of opinion among them as to whether the entire cost should be borne by the employer, or whether a part of the cost of insurance should be borne by the employee. Mr. Green of the A. F. L. suggested that disability compensation be combined administratively with workmen's compensation. Mr. Padway, General Counsel of the A. F. L., believed, as did nearly all labor representatives, in a compulsory system of insurance. He stated the physicians had been criticized too much, and that much was unfounded. The physician has and is rendering excellent service to the community. He must realize that there is some place where he stops, a point beyond which he cannot advance. Beyond that line the government must take up the work. The physician is part of the problem. He must be consulted and have something to say of the plan. He must be an integral part. They must not oppose the plan, because it is coming. He (the physician) must see the handwriting on the wall. He must help devise the plan which will function best.

Specific Recommendations.—Turning to the discussion of specific points. As stated before, the discussion was general as a rule, rather than specific.

Maternal and Child Health. This was apparently accepted as of "primary importance" as stated by the Committee. No definite opposition to the expansion of Public Health Services was presented. Several warned of the necessity of going slow, as success would depend on the development and training of personnel.

Some criticism was directed to the hospital recommendations. Father Schwitala and one or two others questioned the factual data, and he stated he feared it would lead to the replacement by government institutions of the voluntary organizations which had given so much service. Dr. Goldwater thought that the program submitted arrives at its results by methods of calculation that are too simple to be reliable. He stated that thousands of hospital beds are now vacant and that efforts for a more complete utilization of existing resources would materially reduce estimates of need. Experience has shown that generous federal hand-outs almost invariably result in political log-rolling and wasteful expenditures.

Medical Care for the Medically Indigent: The question of "needs" was not as a whole challenged. There seemed to be a general acceptance of the fact that good medical care was not being received by many who could not afford to pay for it.

The subject of insurance perhaps provoked the most disagreement as to methods, but with few exceptions not as to its place in a national program. Thus labor on one extreme wanted a federally controlled compulsory insurance system. The Committee recommended a state plan. A number of representatives of existing voluntary associations thought the solution lay in the extension of voluntary group insurance plans. "Group hospitalization" came in for much favorable discussion, with the suggestion of its extension to include prepayment for medical services.

Capital and Industry: The lack of representatives of capital and industry in the Conference was striking. Huge sums of money were glibly talked about in a casual way that was rather staggering to the medical members of the conference at least. Except for a statement of one labor member that as far as insurance was concerned the "employer" must pay the bill, the problem of where the money was coming from was not mentioned. The idea seemed to be that it was for the technical

interests and consumer to plan the program and Congress to find the means. The only representative of capital who spoke, Mr. Charles Taussig, President of the American Molasses Company, stated "Progressive business will regard an adequate health service as a subsidy to industry, not a burden."

Perhaps the best summing up of the discussion was that of Prof. Winslow of the Yale University School of Medicine near the close of the final session. We quote from his remarks taken from stenographic notes, and uncorrected by the speaker.

"I have met with groups, a good many of them in this very room or part of it, for ten or twenty years, discussing these problems, and I think in the back of our minds all that time was the dream and the hope that something might happen like this Conference.

"Dr. Grulee suggested that we were dealing here with a premature infant. It would be very presumptuous for me to differ on the point of diagnosis with a professor of pediatrics, but I hope he will take the subject back to his clinic and consider very carefully whether it may not be malnutrition, instead of prematurity. (Laughter.)

"I think this infant is older than he thinks, and I suspect that all it needs is a little administration of vitamins CIO and AFL and whatever kind of vitamin they make in the Farm Bureau, to make it a pretty husky child. (Applause.)

"Now I am going to break all precedents of this Conference by talking about the subject in hand, and the report that has been presented (laughter), and I think this Conference has been of extraordinary significance for three major reasons. In the first place, we have had presented to us here a report which is the work of five independent government departments working in cooperation. Now those of you who remember the one-time relations between the Children's Bureau and the Public Health Service will realize that that is nothing short of a miracle. Nearly half the President's Cabinet is represented in these proposals that have come to us, and for that type of coordinative action, as for so many other things, we owe a tremendous debt to Miss Roche. (Applause.)

"The second reason for which this conference seems to me significant is the excellence of the program that has been presented by the staff that has been working for so long upon it.

"This report is notable for the care with which it has been prepared, for its soundness and particularly for its balance. I think it is possible that in the discussions of yesterday and this morning, devoted largely to one or the other of the particular phases, we may tend to lose sight of the interrelationship which is so skillfully woven into that report. This is not a program of health insurance, it is not a program for the extension of medical service, it is not a program for hospital construction; it is a coordinated, complete, interlocking, dove-tailing health program for the nation in which all these things have their just and proper part.

"In the perfection of that program the members of this conference have brought incalculable aid. I am sure that as we read the printed report, even more than in listening to the speeches, we shall find innumerable instances in which practical, important difficulties have been pointed out and in which happier solutions of certain aspects of the problem have been suggested.

"Yet on the whole I think the most extraordinary thing about this Conference is the overwhelming preponderance of opinion in favor of the general objectives and general methods of the report. So far as I can recall, and I have sat here all through the Conference, partly because of the interest of the speeches and partly, like some of you, I think, because this room is air-cooled and the corridor is not air-cooled—a great addition to the success of any meeting—and I have listened to every paper, only one apparent criticism of the data presented has been made, and that criticism is only apparent. Father Schwitala referred to the study that has been made by the American Medical Association indicating that only a small num-

ber of counties in the United States were in all parts more than thirty miles from a hospital. Now that apparently is in conflict with the figures of the Committee, but it isn't in the least because the Committee based its judgment of hospital needs upon the number of beds available per thousand population, and people use beds in hospitals, not hospitals as a whole, and the American Medical Association study simply gives you the number of people within a certain distance of a hospital. On that basis, if there were one 10-bed hospital in the City of New York or the City of Chicago, it would be classified as adequately cared for. Now I don't think even Dr. Goldwater would be inclined to accept that as reasonable or important.

"There have been other suggestions which differed from the general tenor of the report from the standpoint of haste and the rate at which we want to move. Mr. Lee Pressman wants to move much faster and he wants to move more toward federal or centralized control than others. I presume that is because that is the characteristic way in which his temperament works. Dr. Goldwater and Dr. Olin West want to move more slowly, and with less centralization. That probably is the way their temperaments work, and both those points of view are helpful in arriving at exactly the proper pace that is desirable under given circumstances.

"I would like to say just one word about this question of federalization, though it was admirably treated by an earlier speaker today. I am a little troubled sometimes at the assumption that a Federal Government is a peculiar, strange kind of foreign body intruded into these United States by some mistake. I have never been able to regard it that way. I regard the Federal Government like the State government and the city government, and like my Community Chest of which I have for two years been president, as an organ through which I and my fellow citizens can function, and I don't think there is any particular spiritual or moral value about a voluntary or an official agency or a state or a federal agency. The problem is, how can a particular end best be achieved?

"I am an individualist, because I am a New Englander. I like to do things when I can on my own steam. If I can't, I like to do things as a member of my family, or as a member of a voluntary agency in the community, or as a citizen of my city or my state or my nation, and I quite agree that the simplest and most direct way of solving a particular problem should be sought, but I think the evidence presented here has been absolutely overwhelming that individual and voluntary and city and state agencies are inadequate to meet this situation without the help and the stimulus that this federal plan will give to them.

"Mr. Weiss in discussing his attitude about the matter said that he was one of those people who wanted to have his doctor. Judging by the success of *Time Magazine*, I suppose he can (laughter), but the reason why this conference is called is that there are a great many million American citizens who can't have their doctor, and the whole purpose of these projects that have been put before you is to give them somewhat similar opportunities to those enjoyed by Mr. Weiss. (Applause.)

"Now the further reason why this congress is significant is the astounding and thrilling support that has come to its main objectives from the groups that have been represented here. I have, as I say, discussed this thing in this room and in other rooms, but never before has it been discussed face to face with those great agencies that really represent the American people, and when this health program has received, as it has received in general principle and in broad method, the support of both the great labor organizations of the country, of the agriculture of the country, of the business of the country with that splendid phrase, which we never want to forget, of Mr. Taussig's, that 'tax-supported health program was not a tax burden but a subsidy to industry,' and with that other magnificent phrase of his, that 'democracy should be a sword as well as a shield'; when we have the

support of the women of the country, and the parents of the country, and the youth of the country, and the press, that is a fact of the most profound and momentous significance.

"We have, I think, in the course of this discussion made it fairly clear that criticism of the existing situation is not criticism of the medical profession, any more than Dr. Baehr's admirable, just, and sound criticisms of our political force was a criticism of us as individuals. There are in my part of the country many people who don't like anything that is going on today in Washington, but because they do not like the acts of the present administration that happens to be in power, it doesn't mean that they are making an assault on the American home and on George Washington and the Constitution.

"On the contrary, I see in the discussions of this Conference, particularly on Monday, an extraordinarily touching appeal to the medical profession. It has been the boast of the medical profession, and the just boast, and the source of proper pride, that if a woman came with a sick child to an individual physician and said, 'My child is suffering and we want you to care for it,' that he never failed to respond. Now what has happened here this week is that the representatives of millions of men and women in the United States have come to the medical profession as a group and said, 'Our members are sick and suffering and we want medical care for them, and we want means provided by which we can pay.' Is it possible, is it conceivable that that appeal is going to be rejected? I think not. (Applause.)

"I was reading a rather poorly typed manuscript a day or two ago and I came to the title of a reference which I thought read, 'Medical Care Not Now.' I looked more carefully and saw it was in the *Survey* and realized that title couldn't be right (it might have been in some other magazines), and I found the title really was, 'Medical Care But How.' And I thought my mistake rather symbolized our situation. I think with this Conference the whole problem has shifted from medical care not now to medical care but how.

"Now I, like Dr. Davis, do not minimize the difficulties. There are many practical difficulties. I would like to point out that running through all these proposals that have been made, there are as it seems to me two fundamental problems. One is the problem of organizing the medical profession for effective service. It is not now organized effectively for physicians, because physicians are in large measure not where they are needed and it is not now organized in such a way as to give the maximum possible guarantees of quality. That is a professional question. It is a question which must be solved by the medical profession through their medical societies, and perhaps better through their hospital staffs, and by the health officers of the community, but underlying all these problems is that basic problem, that one basic problem of organizing the profession so as to make their services available where they are needed and to keep those services at the highest possible level of quality.

"The other problem, of course, is the question of organizing the profession properly for effective service and to organize the financial resources in the community to make the maximum possible and maximum reasonable payment for that service.

"It is quite clear, I think, that effective methods of organizing the community's contribution to payment can be made without any interference with the standards of the profession and without any interference with the principle of freedom of choice.

"I have great sympathy with the principle of freedom of choice of physician, but I should like to point out that any acceptable definition of freedom of choice of physicians must include the right of a group of patients to choose a group of physicians for their service. (Applause.)

"Any artificial attempts to interfere with that freedom cannot stand.

"Mr. Kellogg in his excellent address yesterday introduced the fable of King Canute. He did not make any application of it; he is much too diplomatic; nor

will I. I do not know who he thought was attempting to hold the tide back, but I do know that I am not of that kind, and that as I think over these three days and the great wave of enthusiasm and devotion to the promotion of national health that has been manifest here, I say, thank God, at last the tide is coming in!'' (Applause.)

In closing the Conference Miss Roche stated that in light of the discussion and suggestions, the Technical and Interdepartmental Committees would move forward to a plan of action. She felt the discussion revealed substantial agreement on fundamental points, and many of the principles set forth in the recommendations. In preparing proposals for legislative action, the Interdepartmental Committee hopes to have the benefit of further counsel from those present as well as others who have not been present. ''I think it should be unnecessary to specify that among those from whom we expect to receive constructive suggestions and aid are the members of the medical profession.''

Borden Veeder.

THE DOCTOR HEARS STRANGE RUMBLINGS.

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Critical Review

SOME PEDIATRIC PROBLEMS OF BEHAVIOR IN INFANCY AND EARLY CHILDHOOD

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INFANCY and early childhood have for a long time been the no man's land of child psychiatry. The personality and behavior problems of older children have for the past two to three decades been studied and treated in mental hygiene and child guidance clinics, psychiatric outpatient departments of some of our large hospitals, and by psychiatrists connected with schools, camps, placement agencies, juvenile courts, and correctional institutions. The developmental and training difficulties of infants, however, did not come to the attention of any of those groups. Valuable contributions were made by psychologists about the normal evolution of early functions and some of their fluctuations but usually not in a manner that would make those observations serve as immediate practical aids to parents and nurses. The few articles on disturbing behavior of infants, however meritorious, were almost lost like drops in the ocean of literature concerning behavior, training, socialization, and parent-child relationship after the third year of life. The psychoanalysts, through retrospective deductions from interpreted material obtained from adults, have built into the infant's, the newborn infant's, and even embryo's "unconscious" a wealth of mechanisms and experiences which have been substantiated about as convincingly as the reports of life after death.

And yet, "life," "behavior," "interpersonal relationship," all that goes gradually into the making of a person, certainly is present from birth. Maternal perplexities, uncertainties, apprehensions may be present then and may have existed even before then. The parents cannot, and should not, turn for advice about their infants' behavior to psychiatrists, most of whom will honestly admit that they have had no experience whatever with infants. The parents expect that advice to come from their pediatricians. For this reason, a review of the work with problems of behavior in infancy and early childhood has its proper place in a pediatric journal.

PROBLEMS OF FEEDING BEHAVIOR

Infant nutrition has rightly been a major issue of pediatrics. The factors of growth, health, and general development are closely interwoven with the adequacy of food and digestion. The process of establishing usable principles of feeding has been accompanied by much controversy, by rigidity and relaxation of rules, by an assortment of dogma, heresy, and skepticism. Attention was so thoroughly focused on *giving* food to infants, that the infants' *taking* of food, or feeding behavior,

had little opportunity left for consideration. Refusal and fussiness that were not directly attributable to physical illness were labeled as nervous anorexia, which in turn was usually treated with more concentration on the food to be given and little, if any, regard for the child to be fed. This neglect of the eating habits of infants eventually came back as a boomerang when psychologists, pediatricians, and parents began to become person-conscious and look in the individual child for explanations of his acceptance or rejection of food. Anorexia, the dreaded *crux paediatrica*, came to be viewed not merely as a pseudodiagnostic alibi but as a definite therapeutic and prophylactic challenge. The last fifteen years have seen a wholesome and, as events have shown, practically helpful shift in the attitude towards eating difficulties of infants and children. Attention to food substances was supplemented by attention to feeding behavior. "Feeding behavior," as Gesell[17] has recently said, "is chiefly concerned with the intake of food rather than with food assimilation. Assimilation, however, may be indirectly affected by the mode of intake, so unified is the personality of the infant and so pervasive is the psychobiology of the alimentary tract. . . . Each child presents an individual pattern of growth and an individual pattern of personality. Although the feeding behavior of infants develops in accordance with certain laws, the expression of these laws takes on unique features in the individual. Therein lies the necessity of individualization in the supervision of feeding behavior. . . . In the diagnosis and supervision of feeding behavior we have an approach to a developmental hygiene which embraces at once the growing body and mind."

Important contributions to this change of front have come both from pediatricians and psychologists. Among the former group, Aldrich[1-3] and Brennemann[6-8] deserve a great deal of credit for doing pioneer work in this direction. Aldrich has had the courage to present his insights to the lay public in a readable and informative book which manages to steer clear of the pitfalls of overpopularization and unnecessary alarm. (Alarm is always unnecessary.) The incidence of anorexia in private pediatric practice has been variously estimated at from 50 to 85 per cent.[21] Brennemann stated: "Anorexia is not an occasional occurrence, an isolated phenomenon in childhood; it is the rule in that very stratum of society in which mothers are lying awake nights planning a gospel diet and the most effective way of administering it. . . . It has been stated that this condition exists only among the well-to-do—that a poor appetite is rare among the poor. My experience does not quite confirm this observation." As a matter of fact, in our own work at the Harriet Lane Home children with feeding difficulties have been referred with about equal relative frequency from the dispensary and the private consultation service, a total of not less than one-fourth of all cases sent for psychiatric advice. "This truly amazing phenomenon, the majority of the young of any animal refusing to eat a diet that is not only scientifically optimum, but as appetizing as culinary ingenuity can make it, can be explained only on a psychologic basis. It is, a priori, unthinkable that it is on a physical basis."[6] Brennemann found the psychologic feature to consist of two principal interrelated components, one to be sought in the environment and the other in the child himself. Obsession with the dangers of overfeeding, undernutrition, and deviation from rigid rules about quantities, percentages, calories, intervals, and stools, and a campaign of frequent weighing and measuring to attain narrowly

delimited standards of "perfection" have tried to make of the infant something of a machine to be oiled with certain kinds of oil only, at certain times only, in a certain manner only, with just so much oil only, and according to specifications provided for all machines, regardless of their special makes and performances. Many infants, not being machines, rebel against this standardizing, "extraneously, arbitrarily imposed authority," inflicted dutifully and carried out to the letter by anxious mothers; the adults' emphasis on eating furthermore supplies the child with an effective tool for his desire for the spotlight and domination of the home.

How imperative and indispensable are those exacting diet prescriptions imposed upon mothers and infants? Clara Davis[10-13] approached this question in a very original way. She subjected three infants of weaning age to a self-selected diet experiment, two for periods of six months each, and one for a period of a year. Having previously had no other nourishment than breast milk, they were allowed to choose without any kind of restriction from a large assortment of ordinary foodstuffs. They were able from the first to select their own diets in quantities sufficient to maintain themselves with apparently optimal digestive and good nutritional results as far as immediate effects could be judged. They were omnivorous and in eating were governed not only by their caloric needs, but showed definite preferences which, however, changed from time to time and were unpredictable. These studies, carried out at the Children's Memorial Hospital in Chicago, were extended to include fifteen children. Cooked and raw, uncombined, unseasoned, and unsophisticated foods were served according to an unvarying schedule of three meals a day, and no food was given between meals. Each child had his own small table and the foods for the meal were set before him on a tray. Children ate with spoons or fingers, depending on ability or preference, and empty dishes were promptly refilled to make sure that the children got all they wanted of everything. Food and eating were never discussed by the attendants in the presence of the children. In this setting, "anorexia, other than as a transient loss of appetite with acute parenteral infection, was unknown among them, all eating heartily with keen appetite day in, day out. It was not unusual for children to eat three or four bananas at a meal or five to seven servings of potatoes or meat. One child a year old frequently drank a quart of milk at his noon meal besides eating other food. Yet none were fat, and all were solid well-built children, healthy and vigorous, presenting no problems in behavior. A few instances of vomiting or diarrhea occurred with an acute parenteral infection, but otherwise there were no digestive disturbances and never any constipation, laxatives never being needed or given to any. The study demonstrated that under the conditions of the experiment and with such natural foodstuffs young children could choose their diets and thrive without adult direction of eating."

In another equally fascinating study, Dr. Davis[12] allowed three infants their choice of four formulas from the end of the first week of life throughout the nursing period. The formulas consisted of (1) a proprietary "reconstructed" cow's milk (Similac), in which there was some readjustment of the fat and salt content and addition of lactose to approximate woman's milk as much as possible; (2) fermented lactic acid milk with 5 per cent of Blue Label Karo corn syrup; (3) a simple milk dilution formula (whole milk, boiled ten minutes, 20 ounces; water, 10

ounces; lactose, 1.5 ounces); (4) an orange juice, egg yolk, sugar, milk, and water formula. One of four bottles of equal make and size, with nipples of the same brand and shape, was offered; when the infant stopped sucking or did not suck, a second bottle was substituted, until all four had been proffered. A bottle emptied during the feeding was refilled to insure that the infant had all he wanted of that formula. The total quantity was left entirely to the infant. Undiluted orange juice was given twice daily. The infants showed individual differences in taste, though the preferences shown were moderate in degree. The most striking feature of their performance, however, was the wide variation in the quantities taken at a feeding. "This pattern of eating behavior, i.e., occasional 'stuffing' and meals of widely varying quantities, is, of course, the natural one not only of mammalian young in general, but also of the breast-fed baby. Furthermore, it is not only an infantile pattern but one that continues to a greater or less degree throughout life. Artificially fed infants appear to be the only large group on whom identical quantities for successive meals are meticulously imposed, and one cannot but wonder whether the comfort of these infants who exercised choice not only of formulas but of quantities and their complete freedom from digestive discomforts and symptoms of any sort were not due rather to the following of this natural eating pattern than to the combinations made by their choices of formulas."

I have reported the Davis experiments in some detail because I consider them as being of fundamental significance. They give scientific backing to the present trend of refusing to sacrifice regard for children's personal needs and domestic tranquillity on the altar of nutritional dogmatism. They make allowance for individual preferences, with strikingly satisfactory results. Confirmation of the early existence of personal differences with regard to food intake and feeding behavior has come from nursery observations made by reliable psychologists and published, among others, by Eliot,[15] Ripin,[22] and Dockeray.[14] An important recent contribution has come from Gesell and Ilg,[17] who reported their work comprehensively last year in a book entitled, *Feeding Behavior of Infants.* The authors made minute studies of infants' eating from the first day of life until the second year and recorded carefully the "foundational patterns" of feeding and related behavior, the motor mechanisms of feeding (basic adjustment, suckling, mastication, swallowing, from hand to mouth), behavior towards nursing utensils (breast, bottle, cup, spoon), reaction to different types and consistency of food, acceptance and rejection, food-sleep relationship, and the interplay between infant and adults in connection with eating. This book is a veritable storehouse of well-rounded information and renders a real service to pediatricians.

Attempts have been made to show how early feeding behavior may affect the development of character and conduct. The use of statistical correlations between feeding methods and later behavior problems or personality traits seems to this reviewer to be of questionable value in situations in which numerous other factors are variously and potently at play. It may be in order to correlate more specific items, such as satiation from breast feeding and finger-sucking, as Levy[32] has done (reported under the caption of thumb-sucking). Beyond that, however, one wonders how many errors are introduced by the neglect of many significant features in the life of the child. Childers and Hamil[9] studied

the emotional problems of 469 children less than 13 years of age "as related to the duration of breast feeding in infancy." Their tabulations seemed to show that undesirable behavior manifestations (of patients referred to the Neuro-Psychiatric Clinic of Harper Hospital, Detroit) were greatest among those who had been weaned between the first and sixth months of life; next in frequency were those who had never been breast-fed; then came the group in which breast feeding had been continued into the "normal" period for weaning; the children in whom breast feeding had been prolonged beyond the eleventh month showed the smallest percentages of undesirable traits. The authors concluded honestly: "The statistical fallacies of this study are recognized, but the comparisons illustrated in the graphs of the four groups are quite interesting." Hill[18] selected from more than 500 consecutive admissions to a psychiatric clinic 172 children and adults (!) "because of the available detailed information regarding early childhood development for special study of the relation of infant feeding, digestive disturbances, and personality disorders." The group was composed of cases in which the breast feeding was inadequate, excessive, or adequate. Hill reached the following conclusions: "Inadequate or excessive breast feeding is undesirable both from the physiological and psychological viewpoints. Both of these extremes in infant feeding are common. It was inadequate in 49 per cent of the cases and excessive in 9 per cent. A strong familial interest in the upper alimentary tract and a faulty maternal emotional reaction to the child are most important factors in functional gastrointestinal and emotional disorders." The thirteen examples cited, of whom three only are children, are so heterogeneous and offer such extremes of schizophrenic, manic depressive, alcoholic and psychoneurotic conditions, that the jump from infant feeding to personality disorders appears to have skipped all sorts of biographic data certainly not less life-shaping than the feeding in infancy.

Mohr's study[20] keeps itself on much firmer ground. In an investigation of sixty-six children presenting problems of eating behavior, he stressed the importance of the emotional relationship between mother and child and advocated early instruction of the family on the part of physicians, for "failure to cope adequately with this problem implies a likelihood of similar unsatisfactory modes of behavior in other fields of activity." R. M. and H. Bakwin,[4] in a recent discussion of the prevention of anorexia, stated: "Anorexia during the first months of life, though usually organic in origin, often has a basis in the psychologic environment. The most potent psychologic factor at this early age is an agitated, uncertain parent or nurse. Young infants appear to be particularly susceptible to this attitude and react with restlessness, disturbed sleep, excessive crying, anorexia, and often vomiting."

Summary.—During approximately the past ten years, attention to the average and the undesirable feeding behavior of infants and children has been added to the interest in the foodstuffs to be given. Anorexia which is not solely due to physical illness is now recognized as the result of the combined behavior of the infant who is fed and the person or persons feeding him. The Davis self-selection experiments have tended to do away with nutritional obsessiveness, at the same time without losing sight of the sound basic principles arrived at in many years of patient pediatric work in laboratories as well as in the nursery. The pediatricians, encouraged by their personal experiences, the insight of

leaders in their own ranks, studies made by psychologists and the fundamental work of Gesell, have come to include in their practice the prevention and treatment of faulty feeding behavior as part of the physical and mental hygiene of infancy and childhood. Education of the parents in matters of early feeding behavior is becoming in an increasing degree a part of the pediatrician's task.

THUMB-SUCKING

The great concern of present-day mothers over the thumb-sucking of their offspring is largely due to the warnings of alarmists in the ranks of dentists and psychologists. Prior to those scares, the habit received but scant notice from parents, pediatricians, or anyone else. Even folklore, seizing so promptly upon every portion and function of the human body, attributing great significance to such things as sneezing and yawning and firmly believing in the worm etiology of nose picking or grinding of teeth, has failed to consider finger-sucking as worthy of its attention. Several famous artists depicted children with thumbs in their mouths to give them an expression of serene tranquillity. Mazzini[38] and Bragman,[26] who compiled notes on thumb-sucking in productions of art, saw it presented in paintings and sculptures of Ghirlandajo (*Adoration of the Magi*, 1488), della Robbia, Borgognone, Credi, Lippi, and other Italian masters of the early Renaissance. The notion that it is bad or harmful did not arise until the end of the last century.

Since that time, dentists and especially orthodontists asserted that thumb-sucking results in malformations of the jaws and palate. Parents were therefore admonished to do everything within their power to curb a child's performance so injurious to his future mastication and physiognomy. All sorts of mechanical devices were invented, publicized, and marketed to keep the little thumbs from reaching the mouth. Illustrated articles in dental and pediatric journals[23, 25, 28, 40] described ever new varieties of cuffs, muffs, Elizabethan collars, and modified strait jackets. People who refrained from hampering children's movements took refuge to ill-tasting substances which were smeared on the fingers in order to preclude sucking and subsequent damage to the configuration of the jaws. Later investigations tended to show that the shape of the palate does not become affected by thumb-sucking. Temporary malocclusion may occur but does not become permanent. Lewis,[37] in 1930, concluding the observation of 170 children over a five-year period, found some degree of malocclusion of the deciduous teeth in twenty-four out of thirty thumb-suckers; if the habit had been stopped before 6 years of age, the deformity corrected itself spontaneously. Hence, early sucking certainly did not produce serious or lasting disfigurements. Yet it is mostly the wailings alone that reach anxious mothers, and not the calming reassurances. Popular books on the care of infants continue to discuss the harmful results of thumb-sucking.

Parents are also besought to beware of the germ danger. Says a famous psychologist who has become a very widely read mentor for mothers:[41] "From the standpoint of the child the matter is serious. Physicians tell us that some 90 per cent of diseases due to germs find their way into the body through the mouth. The child with its mobile hands gathers germs everywhere. Next it puts the hands into the warm, moist mouth. The germs are thus given an ideal breeding place." If a mother is not duly scared by that, she may read on as the text continues:

"If persisted in for long at an early age before the bony, tendinous, and muscular tissues harden, the mouth becomes misshapen and the fingers and hands are changed in their contours. There are many other bodily changes which may occur, such as interference with the proper growth and position of the teeth." You can see a frightened mother, after the perusal of this or similar bits of information, run to her physician, imploring him to save her thumb-sucking infant from a life of disease and ugliness, with misshapen mouth and teeth and fingers and hands, with his mouth a culture medium for germs introduced by the thumb! The mother does not have a chance to read statements in scientific journals, such as this:[4] "There is no evidence to indicate that thumb-suckers are more susceptible than other children to gastrointestinal disturbances, infection, or stomatitis."

As if the overemphasis on physical effects were not enough, parents have been harassed by psychologists. Said Watson:[41] "The effect of thumb-sucking upon the child's personality is the most serious aspect of all." According to him, "millions of mothers who are almost criminally careless" use a pacifier to keep the child quiet and, if they let their offspring suck the thumb (a "highly unsocial act"), they are "condemned in progressive communities." And, of course, he did not forget to tell mothers that thumb-sucking is "in part a sex response closely akin to masturbation." This wisdom had come to him from psychoanalysis. Freud,[27] in the second of his *Three Contributions to the Theory of Sex*, chose thumb-sucking "as a model of the infantile sexual manifestations." He believed that "association of the manifestations into which we have gained an insight through psychoanalytic investigation justifies us in claiming thumb-sucking as a sexual activity." Since not all children suck their thumbs, he assumed that "it is found only in children in whom the erogenous significance of the lip zone is constitutionally reinforced. If the latter is retained in some children they develop into kissing epicures with a tendency to perverse kissing, or as men, they show a strong desire for drinking and smoking. But should repression come into play, they then show disgust for eating and evince hysterical vomiting. By virtue of the community of the lip zone, the repression encroaches upon the instinct of nourishment." Thumb-sucking is viewed as a form of autoerotism, the sexual aim being under the control of an erogenous zone. If "autoerotism" simply means derivation of pleasure from certain sensations of the body, then the pleasure derived from sucking is autoerotic by definition. The hedonic component of many of the manipulations of the body cannot be denied or minimized. Nor does one wish to deny that some degree of lack of self-control is common to all of them. Homburger[29] has referred to the sensations which accompany them as "perverse pleasure sensations." But this is something altogether different from attributing sexual significance to the habit and even identifying it with "larvated masturbation." Psychoanalysis, though, is probably not to be blamed directly for the extent to which some of its adherents have gone in analyzing the habit of thumb-sucking. Melanie Klein,[31] reporting the case of six-year-old Erna, told a listening world that the little girl's thumb-sucking "was caused by phantasies of sucking, biting, and devouring her father's penis and her mother's breasts. The penis represented the whole father and the breasts the whole mother."

The etiology of thumb-sucking has been approached from still another angle. Levy[32, 35] has in an interesting study come to the conclusion that in a majority of instances it is due to insufficient lip movements or incompleteness of the sucking phase of the feeding act, regardless of the type of feeding (breast, bottle, or mixed). He named as the most frequent causative factors: (1) spontaneous withdrawal from a too rapidly flowing breast or bottle; (2) forced withdrawal from sucking at the termination of too short a period of time; (3) changing feeding schedules with increasing intervals between feedings and diminished duration of the feeding time. Each nursing period, according to Levy, begins with the child tense and restless because of hunger. As the feeding continues, he becomes relaxed, and after a fully satisfying meal he is sufficiently relaxed to fall asleep. If, however, he is not fully satiated, he may suck his thumb or fingers, thus maintaining something of the pleasures of nursing until he falls asleep. There can be nothing seriously undesirable about this form of behavior, provided it does not become chronic. But if the feeding is not entirely satisfactory, there is danger that each meal will so frequently be followed by thumb-sucking that the act will become thoroughly habitual. Levy[33, 34, 36] subsequently extended his investigations to dogs, calves, and chickens. If the feeding act was disrupted before the point of satiety was reached, a sucking habit resulted in dogs in the form of licking of the paw or the body of another dog, besides sucking of various inanimate objects. In calves, the licking habits concerned the ears of other calves, painted boards, clothes, anything suitable for licking. The pecking behavior of chickens raised on a platform of wire mesh (and that of turkeys) was found to follow the same law of instinct satiation as in the studies of sucking behavior. Levy stated that the percentage of finger-suckers was highest in infants fed every four hours, less in a group fed every three hours, and least in a group fed irregularly. On the other hand, Gesell[17] was led by his own observations to remark that "there are so many exceptions to this relationship that it cannot be set down as a general factor."

Gesell[17] found finger-sucking to be associated with hunger during the first few weeks of life, but then receding at the time when the postural development does not permit the hands to be readily brought to the mouth. By the third month, this movement becomes easier again, and the fists are sucked prior to and later also after feeding. In the fourth month, the sucking in many cases appears throughout the day. The infant "probably relieves the pain" from local irritations that may be present weeks or months before actual eruption of the teeth "and possibly aids dentition by mouthing his fist." The successive teething episodes seem to exacerbate the hand-to-mouth response. "With those who later become persistent thumb-suckers, the degree of the sucking may markedly lessen or even vanish between the teething periods. All of this behavior suggests that mouthing may play a part in the developmental economy of teething." Fatigue and frustration are other inciting factors. Gesell reported a most interesting observation. When an overzealous mother, in her efforts to train her child in toilet habits, places him on the toilet many times when he has no occasion to use it, the thumb-sucking child usually does not resist the procedure but promptly begins to suck his thumb and keeps it up contentedly for the duration of the séance. However, if he spontaneously asks for the toilet, he will not bring his thumb to his mouth.

Summary.—Thumb-sucking in infancy has been made the object of parental scare by insistence on its damaging effect on dental occlusion, the infectiousness of the sucked finger, and its identification with autoerotism. Sober observation has tended to remove these scares and thus free infants from all sorts of frantic attempts to break them from the habit. Pediatricians can help frightened mothers by explaining to them the relative harmlessness of a short period of indulgence. Reasonably well-fed and well-occupied children will sooner or later give up the habit without the much more harmful battle introduced by the application of devices which hamper their movements. Calm removal of the thumb from the mouth, substitution of play interests for the pleasure derived from sucking and absence of unwarranted alarm constitute the best method of treatment of thumb-sucking in infancy.

THE SO-CALLED AGE OF RESISTANCE

The earliest expressions of anger, resentment, remonstrance, disobedience, spitefulness, stubbornness, and destructiveness, the first refusals to conform to feeding, sleeping, and elimination routine, and the beginnings of any kind of willful resistance to adult direction and training have been said by many investigators to appear during the third year of life. This type of behavior, succeeding a biennium of relative submissiveness, has been frequently referred to in the literature as a characteristic manifestation of the "age of resistance" or "period of negativism"; German authors speak of it as the "spite period of childhood." It is generally stated that it lasts several months sometimes between the ages of 2 and 4 years. Thom[54] spoke of a group of children who develop what may be termed "contra-suggestibility" from 3 to 5 years of age. Many psychologists became first aware of this contrariness by the observation of the frequency of children's refusals to cooperate in mental test situations. Binet[44] mentioned the difficulties encountered in trying to obtain the cooperation of normal 3-year-old children, attributing them either to timidity or to "bad mood" and "bad will." Gesell[17] remarked that "the 2-year-old child is considered to be the most resistant to psychological examination." Reynolds[52] found in a study of 229 preschool children that the peak of negativism was at or below 2 years of age, with a gradual decrease from then on. The mean of the negativistic scores of the 2-year-old group was 6.44 and that of the 4½-year-old group was 2.26. The correlations between life age and negativistic score were higher than those between mental age and the score. There was no special difference shown in the reaction patterns of the refusals made by the different age groups, the distinction being one of frequency rather than of degree or kind. The 2-year-old child was more apt to refuse to cooperate on a situation but when he did refuse he showed the same kind of behavior as the older children. The 4-year-old subject was less likely to refuse, but when he did his behavior pattern was similar to that of the younger children.

Levy and Tulchin,[50, 51] who observed 983 infants and children during testing, found the manifestation of resistance to be typically pronounced at 18 to 23 months in girls and at 30 to 35 months in boys, yielding gradually with age in both sexes. They tabulated the resistance patterns during mental tests of 110 children ranging in age between 6 and 54 months. The earliest resistances noted, at 6 to 7 months, were crying and clinging to the mother. All reactions recorded before the four-

teenth month were crying and withdrawal movements denoting some relation with the mother. At 16 to 17 months, assault reactions directed towards toys or the examiner and head shaking and verbal objections made their first appearance. Latest to arrive were more complex modes of behavior, such as slapping movements without slapping or walking back to the mother in the midst of the test. Crying, most frequent in the first year, gradually diminished in frequency with increasing age. Simple crying after two years and withdrawal reactions (looking away, covering the face, hand movements) occurred oftener in girls, clinging to the mother oftener in boys.

The majority of authors consider the resistant behavior of preschool children as a normal feature of child development. Thom[54] said: "The negativistic phase of the child's life is recognized as being a normal reaction occurring in the process of growing up. It is the period when the child begins to assert his own personality, when he resents domination by others. This is a natural and healthy reaction." According to Helen Woolley,[55] "negativism constitutes a very frequent stage of development in very young children. It seems to be a natural step in the development of personality. When a child begins to get a feeling of himself as an independent agency, he enjoys trying out his powers." Some attempts at accounting for the resistance have led the authors far afield into theoretical realms. Haeberlin (quoted by Benjamin[42]) was probably the first to compare the infantile remonstrances to the sulkiness and sullenness observed in the early part of the second decade. He was apparently so struck by certain resemblances that he spoke of this phase as the "first puberty." Charlotte Buehler[45] also found analogies between puberty and the so-called age of resistance, consisting chiefly of hostility to the environment and at the same time the formation of strong attachments. She concluded that the similarity indicates the presence from 2 to 4 years of age of a first spurt of sexual development, which then subsides to be resumed at the time of pubescence. A strange interpretation came from Busemann.[47, 48] He began with the assertion that the existence of the "spite period," which according to him begins at about 27 months of age, is an indisputable biologic fact. Like the sucking mechanisms and the instincts related to them, it is anchored genetically and provided for in the anlage. As a matter of fact, Busemann counted five different stages of resistance in the course of childhood and adolescence, the first between 2 and 4 years, the second at about 6, the third between 8 and 9, the fourth between 12 and 14, and the fifth from 16 to 17 years. Nature, he argued, has intended for women a birth rhythm with about three-year intervals between the arrivals of new offspring. If, contrary to this prescription, the next child fails to appear on schedule, the existing youngster suffers from a "luxuriant educational activity" on the part of his mother. She has enough time on her hand to will and act for the child, who in turn having developed his own volition and sense of power rebels against this with stubbornness and spite. Hence the only child is especially likely to go through the five "cycles of excitability," the tempo and course of which are said to be the "biological functions of the maternal birth rhythm."

The infantile period of resistance has been accorded particular significance by Benjamin,[42, 43] who saw in its manifestations and management a most important factor in the development of childhood neuroses

and the determination of a child's personality formation. Mention of a connection with future character traits had been made previously by Hetzer,[49] who stated that the absence of any negativism in a 2- to 4-year-old child may result in weak-willed meekness. Benjamin, like others (Busemann, Levy, and Tulchin), felt that the display of resistance is evidence of an inherent behavior pattern: "Anlage is one of the most essential genetic factors. Differences of reaction forms are based on variations rooted in the anlage." Benjamin took the spite period most seriously as a phenomenon very closely related to morbidity. He wanted a sharp line drawn between normal behavior during that age, about which he had a very little to say, and psychopathologic conditions, to which he assigned the role of a distinct nosologic entity. The basic disturbance lies in the child's failure of adaptation to his environment, due to insecurity and anxiety. His difficulty of adjusting to the task of growing into relationships with other people and the acceptance of values determined by them leads to a state of disorientation, hostile refusals, and isolation, with aversion to cleanliness and to the acquisition of functions commensurate with his age. Hence, for example, come the persistence of enuresis and disorders of speech. This failure of adaptation leaves three possible avenues open to the child: developmental standstill, even to the point of regression to a previous stage of existence in which there was a greater feeling of security; introversive turning away from reality to find consolation in thumb-sucking, masturbation, and rhythmic body movements (such as rocking, head rolling, jactatio capitis nocturna); and spiteful rebellion, resembling the fluttering of a caged bird or the bewildered agitation of an adult in a panic situation. Out of the latter mode of reaction arise feeding problems, vomiting, rebellious wetting and soiling, destructiveness, breath-holding spells, and temper tantrums. A neurosis is characterized by the unnaturally protracted duration of the spite period and has its origin in a combination of social contact disturbances, partial inhibition of psychic development, inner insecurity, and faulty training. Although the rebellion seems to come as a sudden change, two-thirds of Benjamin's 205 cases presented difficulties from the first few months of life, expressed through restlessness, abundant crying, vomiting, constipation, pylorospasm, and stereotyped movements. Because of the etiological significance of the spite period as the basis for later neurotic conditions, Benjamin urged early prophylaxis and treatment not of the symptoms alone but of the total person. His case illustrations depict various problems of preschool children, which are much too readily interpreted as outgrowths of the spite reaction, though they contain ample evidence that many other factors are at play.

Those who believe in the existence of a circumscribed period of resistance have adduced support from some observations made by child psychologists. William Stern[53] and Karl Buehler[46] have noticed independently that a child's first "No" has a volitional meaning and that the significance as a simple denial of fact appears several months afterwards. The nearly uses of "No" mean: "No, I won't do that," "No, that is not to be." A child may have learned to scream "No, no" very energetically when a toy is taken away from him. But for another two or three months, although he can quite correctly show his hands and eyes, he is unable to say "No" when his hand is touched and he is asked, "Is

this your little eye?" Similarly, the volitional "I" precedes its intellectualized use even by a longer time, approximately five or six months. Stern's two eldest children said "I" for the first time at 24 months of age. When one was given a ball, the other said, "I look for ball, me too." But not until 30 months of age was "I" employed in connection with a statement of fact, such as "I am small."

Whether a child's first remonstrances be regarded as an exquisitely specific, anlage-determined, circumscribed phase of infantile development or as the beginnings of self-awareness and self-assertiveness, much will be gained if parents could be prepared for those early negations and refusal practices as something to be looked forward to as signs of normal healthy evolution. They are useful functions of the growing individual that contain the nucleus for sound criticism, competition, and the preservation of self-dependence and self-respect. This attitude would help to remove from children trying to orient themselves in interpersonal relationships the odium of disobedience and contrariness and emphasize the constructive socializing value of self-assertion. The practice of meeting resistance with counterresistance only tends to make of the home a field of battle between the youngster and his elders. A child needs the same good-natured aid and encouragement in finding his place in the family group as he needs in his first attempts at walking, self-feeding, going up the stairs, or climbing on a chair. No harm is done if the petty and irrelevant "No, no" and "I won't" replies are disregarded, if at the same time the more important matters of daily routine and habit regularity are insisted upon with gentle firmness. A child's right to resist unreasonable demands should be acknowledged. Parental domination that wishes to break a child's will and keep him turned on like a mechanical toy, parental indulgence that shrinks from crossing a child's will with the excuse of his frail, delicate, nervous condition, or, out of sheer convenience, the extremes of tyranny and excessive leniency, should be equally discouraged.

Summary.—At the end of the second or at the beginning of the third year of life, children acquire the meaning and application of negation, which is added to their reactive equipment. This acquisition is a normal feature of infantile development. Much of the parent-child relationship for years to come, much of the child's contributions to the family life, much of his character formation depends on the adults' attitude to, and management of, those early negations, refusals, remonstrances, and resistances. Impatient adult counterresistance is apt to bring about an exaggeration and perpetuation in the child of a type of behavior which is a natural and desirable phenomenon to begin with. The one extreme of uncomprehending insistence on strict immediate obedience with harshness and violence often brings on spite and a long war, in which the child uses temper tantrums, refusal to eat and go to bed, and elimination caprices as handy weapons. The other extreme of ready "giving in" provides the child with a means of domination of the family, making use of the same symptoms as "spoiled child reactions." Recognition of this natural phase of child development will help pediatricians to prepare mothers for its appearance, explain to them the early negations and refusals and introduce a type of management that would avoid parental despotism on the one hand and parental submission on the other.

THE MENTAL HYGIENE OF INFANCY

The mental hygiene of infancy lies entirely in the hands of pediatricians, who are the parents' first advisers in matters of child health and behavior. Yet the literature, which is so rich in suggestions with regard to older children, offers almost nothing that could serve the pediatricians as a practical guide. The article by R. M. and H. Bakwin[4] offers a helpful departure. Kanner,[56] in a recent article, tried to present to physicians the principles of mental hygiene during the first 2 years of life. The following passages are quoted from this article.

The interrelationship between an individual and his surroundings begins on the very first day of life and keeps increasing in variety and complexity. During the first two years the progressive unfolding of the inherent potentialities of the species transforms the infant from a passive, helpless, inarticulate being into a more and more differentiated little participant who walks, feeds himself, controls his eliminative functions, comprehends gestures and spoken language, forms words and short sentences, and becomes an active somebody to be reckoned with. Some of this unfolding comes from within; growth, locomotion, the formation of vowels and consonants are in the main independent of educational efforts. The chief danger to the normal progress of these functions lies in hazards to bodily health. The ancient adage, *Mens sana in corpore sano,* still holds true. Attention to physical well-being is therefore one of the principal pillars of mental hygiene. The direction taken by the development of many other functions depends to a much larger extent on the molding forces of the infant's environment, that is, the influences of his home. Hence the considerations implied in the slogan, *Mens sana in domo sana,* constitute the second pillar of the mental hygiene of infancy and childhood.

Child training works towards socialization, for which the groundwork is laid at the beginning of life. Adequate socialization hinges on the establishment of relative self-dependence, security, and conformity. The family physician, through his knowledge of the home and the confidence invested in him, can contribute a lion's share to the smooth introduction and maintenance of these features. As the parents' natural adviser consulted in all matters pertaining to the infant's health, he is in a strategic position that allows him to guard somatic developments, supervise home training, and inculcate sound attitudes.

The development of *self-dependence* is hampered by parental overindulgence and oversolicitude, the behavior commonly alluded to as "spoiling." Spoiling is made up of feelings and actions representing parental needs that may arise from various sources, such as the preceding death of a child, economic, marital, or health features precluding the birth of other children, the void created by the substitution of unsatisfying housework for the richness of a previous social or vocational life, overcompensation for the displeasure accompanying the arrival of an unwanted child, or memories of an unhappy childhood resulting in a desire to smother the child with excessive coddling and protection. A mixture of anxiety, puzzlement, impatience, and inexperience centers the family's attention on the infant's nutrition, sleep, and elimination. Weaning from the breast and the bottle is delayed. The child is not given an opportunity to learn how to feed himself. The meals become tragicomic events with coaxing, cajoling, threatening, and bribing by the adults, and refusal, gagging, and even vomiting on the part of the child.

Learning how to sleep through a whole night is made impossible by the parents' habit of jumping up at the infant's slightest whimpering, carrying him about the room or rocking his cradle. Bowel overconcern resorts to purgatives, suppositories, and enemas. The child, not left alone for a minute of his waking time, fondled and handled and shown off incessantly, does not have a chance to develop the socializing responsibilities commensurate with his age and remains physically and emotionally overdependent on his elders. The well-known spoiled infant syndrome of anorexia, insomnia, constipation, and attention-getting intrenches itself more and more firmly. This failure to establish a reasonable degree of self-dependence, if continued unabated, may lead in preschool age, during the school years, and even later to disturbing difficulties of adjustment.

The development of *security* may at an early age be interfered with by inconsistencies in the display of affection and recognition of achievement, emphasis on real or anticipated shortcomings, instillation of fear and confusion regarding authority. The average sensibly managed infant is happy and secure and as yet untroubled by "the slings and arrows of outrageous fortune." As the temperature of his baths should be neither too hot nor too cold, so should parental affection normally steer clear of the extremes of explosive demonstrativeness and chilly rebuff. Approval of success and encouragement in the face of occasional failure during the first attempts at walking, talking, self-feeding, handling breakable objects, meeting strangers, etc., help to impart to the infant a sense of progress and self-confidence when confronted with ever new tasks. But sometimes parental frustrations, overambition, overconscientiousness, or resentment of the child-training duties as annoying inconvenience lead to sternness, perfectionism, fault-finding, undeserved punishments, and nagging which make the child uncertain of himself and instill timidity, dread of his elders, and lack of self-assertion. The infant is being lectured to and reasoned with in terms which he does not and cannot comprehend and is then reprimanded for disobedience if the sermon has had no results. Constant corrections of initial hesitation in reporting his experiences with an as yet inadequate vocabulary may cause him to become speech conscious and start him on the road to stuttering. The parents' dissatisfaction with his left-handedness may make him miserable by their methods of enforcing a change of handedness. Their agitations about his thumb-sucking or touching his genitals may fetter him with all sorts of mechanical devices. Beating, bogey man threats, and the custom of locking him in a dark closet for punishment may introduce strong and disturbing fears. Under such conditions an infant cannot possibly be expected to develop a healthy sense of security. This is made even more difficult by the frequent inconsistency with which the same act, dependent on the mood of the moment, is tolerated at one time and severely rebuked at another. Besides, differences in the temperaments and attitudes of the parents and other adults in the household often create in the child a confusion of authority when the same behavior is condoned by some and turned into a great issue and censured by others.

The development of *conformity* depends mainly on the introduction of conventional manners, emotional control, and a give-and-take attitude. The first two years are the best time to train ("condition," if you wish) a child for habit regularity. Setting certain times for the

meals and, in the second year, naps and night rest, and the use of the toilet offer the earliest opportunities for the establishment of routine, which is often hindered by parental overindulgence, laissez-faire negligence, or peculiar pseudomedical notions that turn an infant into the central object of his mother's hypochondriasis. The latter is often fostered by fear of inheritance of some relative's disease, superstitions about prenatal marking of the baby, difficult labor or birth or some early illness. The child, branded as sickly, frail, and delicate, receives a considerable amount of overprotection and is suspended from all reciprocal obligations. On the theory that sickly children should never be crossed, he is suffered to dominate the family, take toys away from his siblings and playmates, provided that he is allowed to have playmates, refuse violently to let them play with his own toys, eat, sleep, and soil himself whenever he pleases and destroy anything he wishes to destroy. Improper adult example renders him even more unmanaged and unmanageable. It is a fact that infantile breath-holding spells and temper tantrums are staged mostly in homes where unchecked emotional outbursts are common occurrences and the infants' own upheavals are met with yelling, hitting, and the dreadful habit of emptying a pitcher of cold water over him. The strange combination of giving in, screaming, spanking, and faulty habit training prevents the establishment in the infant of conformity, that is, good manners, sensible use of his emotional equipment and sharing.

Summary.—The family physician can help parents considerably in the mental hygiene of their children by trying to understand, inform and reassure them. He will not attain this purpose by blaming and scolding them and telling them in a general way not to pamper, worry about, or be impatient with their offspring. The desire to understand implies listening to what the parents have to say. An attentive ear will not fail to get the preoccupations, concerns, solicitudes, frustrations, and erroneous beliefs underlying unhealthy management and training. The average mother wants and needs enlightenment about the child's state of health, about what to expect and not to expect of him at a given age.

Herein lies a great challenge to the modern physician who is the only person privileged to administer mental hygiene during the first two years of life and steer the child in the direction of self-dependence, security, and conformity, in other words, in the direction of adequate socialization and good mental health.

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Proceedings

EIGHTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

DEL MONTE, CALIF., JUNE 10 AND 11, 1938

Round Table Discussion of Nursing Care in the Newborn Infant

Chairman: Dr. Jay I. Durand, Seattle, Wash.
Assistant: Dr. Amos U. Christie, San Francisco, Calif.

CHAIRMAN DURAND.—The probable reason for the choice of this subject for a round table discussion this year was the epidemics of diarrheas which have broken out in the nurseries of lying-in hospitals in various parts of the world. With this fact in mind, Dr. Christie and I have decided not to consider many conditions such as asphyxia, hemorrhagic diseases, and prematurity, in which the nursing care has been well covered in pediatric literature and shall confine our discussion largely to nursery technique in the newborn infant.

Beginning with the surgery, it should be noted that there has been great improvement in hospitals, but I believe that the last department of the hospital to receive attention has been the newborn nursery. The patients are inarticulate and defenseless or they would not tolerate the crowding, lack of proper heat regulation, rough garments, and shortage of nurses which so often occurs there.

There is a general awakening to the conditions and more has appeared on the subject of nursery technique in the medical and nursing journals during the past two years than during the preceding ten.

There has been a very definite reduction during two decades in the incidence of mouth, skin, umbilical, and intestinal infections, perhaps some reduction in respiratory infections. While there still were too many hospital acquired infections and deaths, we seem to be progressing. Then an acute communicable disease of the newborn infant made his appearance in the nurseries of many of our well-conducted hospitals. Since this infectious enteritis affects only the newborn patient, it seems an astonishing fact that outbreaks have been reported from such widely separated points as New York, Chicago, Buffalo, Memphis, and Seattle. The etiological agent is so far undetermined, but the symptomatology, progress of the individual case, course of the epidemic, the 50 per cent mortality, and post-mortem findings leave little doubt that it is the same disease. The New York Board of Health has investigated twenty-seven outbreaks in three years up to December, 1937. It has been made a reportable disease, and stringent measures for its control and prevention have been put into effect.

When a case is discovered there is no temporizing. The obstetrical ward of that hospital is closed, all suspected cases isolated, and as soon as the newborn infant can be discharged, the nursery is thoroughly renovated.

Regulations covering all lying-in institutions and newborn nurseries have been put into effect.

These regulations which were published in an article by Dr. William H. Best, Deputy Commissioner of Health in the *Journal of the American Medical Associa-*

tion, April 9, 1938, seem very exacting and perhaps unnecessary in some of their provisions, except in the presence of an epidemic.

They show much thought and painstaking care in their preparation, cover every point in the conduct of the nursery, but, to me, seem to be rather a guide to perfection than an enforceable set of health regulations to control all nurseries.

These regulations and the technique set up by Gladys Dick at the Cradle, as described by Louis Sauer in the JOURNAL OF PEDIATRICS, 1935, furnish the best texts I have found for the conduct of the newborn wards of an obstetric hospital or the teaching of their nursery technique.

Care of the Skin in the Newborn Infant.—The skin of the newborn baby is an extremely delicate and sensitive tissue. Very slight irritation will produce an erythema, and infections are extremely common unless great care is exercised.

Drugs administered to the mother and toxins in the maternal circulation are the cause of some of the irritations. The clothing often roughened and hardened by prolonged use and laundering is responsible for some cases. Washing in solutions, either alkaline or acid, will lead to irritations. Water, oil, and ointments are irritating to some skins. Such erythemas are short-lived and comparatively unimportant except for the concern they give the mothers and because infections are more frequent in infants in which they occur. These infections vary from an occasional bleb or pustule to the large multiple blebs of a virulent impetigo or pemphigus neonatorum.

Some of the more severe conditions are the following:

Intertrigo.—This occurs where skin surfaces are in opposition, especially in the presence of moisture and excessive heat. Air conditioning and heat control of the nurseries, avoidance of excess in clothing but care that a layer of nonirritating clothing is up under the arms, avoidance of excessive zeal in washing, wiping, and rubbing these surfaces, and supervision of the solutions used in the laundry will go far toward prevention.

The Circumcision Rashes.—An infant's skin is sensitive to the attendant trauma, to antiseptic solutions, vaseline and oil, and the secretions which result from the operation, and a fine papular rash with minute vesicles occurs quite regularly on the surrounding parts. In the absence of secondary infection, this heals quite promptly with a variety of treatments. Exposure to the air with heat from an incandescent bulb at a safe distance works very well, as it does also for irritation of the buttocks. A dry dusting powder composed of calomel, talcum, and zinc in proportions of parts 3, 2, and 1, is an assistance in preventing and curing mild infections.

The infections in the newborn skin may be acquired in the passage through the birth canal but are generally due to the hands of nurses, physicians, and mother. Washing the hands before touching any infant should be enforced in every nursery, and the actual skin-to-skin contact between these hands and the skin of the infant should and can be reduced to a minimum. The dry technique later to be described is of great assistance.

The occasional small isolated bleb or pustule is the mildest of these infections. It occurs occasionally in every nursery and in many cases will not spread on the child or to other infants if reasonable care is exercised. Breaking the top and touching with gentian violet or mercresin and applying the dusting powder will heal most of them in two days. Whether isolation of this infant is necessary, I do not know, but it is generally done.

Outbreaks of virulent pemphigus neonatorum have greatly reduced in recent years, but I have vivid recollections of several severe outbreaks. In these epidemics blebs up to two or three inches in diameter raised the superficial layer of the skin, often a considerable portion of the body was involved, and deaths occasionally occurred.

The worst and most obstinate epidemic which I remember occurred when a nurse from a neighboring city came to take care of a sister who was confined in one of our hospitals. About the third day a severe pemphigus appeared on the baby and rapidly spread in the nursery. The nurse told me that the last two babies she had cared for developed the infection and that in consequence she had taken no obstetric cases for the preceding four months. The infection had evidently persisted in her clothing or possibly in an infected sinus during this interval. This epidemic proved extremely obstinate, and in spite of opening three new nurseries while old ones were renovated and painted, sporadic cases appeared, though growing less virulent for weeks.

For the ordinary pyodermias ultraviolet irradiations are very useful in preventing the extension to new areas of the skin and in treatment. They may be a helpful prophylactic measure in sterilizing the skin of babies which may have been exposed to the infection.

In connection with the care of the skin I should like to discuss the "dry technique." In 1931 this practice was instituted by Dr. W. F. Patrick in the White Shield Home of Portland, where approximately 100 babies are born annually, and it has been continued since that time. During the past few months I have visited hospitals in Portland, Seattle, and Vancouver where this technique has been established from one to seven years and I am convinced of its value.

Two reports describing this procedure and the results have been published during the past year. One is by Dr. Heyworth N. Sanford of Chicago. Covering a six-year study of 3,500 infants born in the Presbyterian Hospital, it gives the incidence of skin troubles during the years from 1930 to 1936, inclusive. A certain regime was followed: For two years 2 per cent ammoniated mercury inunctions were first given, followed by daily baths with castile soap and water; for one year, ammoniated mercury at birth followed with subsequent olive oil baths; one year, no antiseptic at birth and only olive oil baths; one year, a commercial antiseptic baby oil used exclusively; one year, only olive and mineral oil used; and one year in which the skin was untouched for nine days except to wipe off any excessive blood. The largest number of infections occurred during the period when ammoniated mercury was used, the largest number of skin irritations during the year of commercial oil application, and the best results of all during the past year when the skin was left practically untouched.

The second report is by Dr. L. Howard Smith of Portland, Ore., and covers the experience during two and a half years in nonbathing and nonoiling newborn infants at the Multnomah County Hospital of Portland, Ore. During this period only two of 1,734 babies developed pustules. These were single lesions and were treated with the calomel dusting powder and healed within thirty-six hours.

The procedure is simplicity itself. Excess of blood is gently wiped from the infant's head and meconium from the buttocks with sterile cotton balls, when the baby is brought from the delivery room. Care is taken not to remove the vernix. If the blood has dried, a little warm water may be necessary. The child is clothed and placed in the crib. Warm water is used to clean the buttocks following stools. The clothing is changed daily, but there is no bathing or oiling.

I quote Dr. Smith: "Within twelve hours after birth the infant's skin is clean, and the vernix has disappeared. Unless one has witnessed the phenomenon, this miracle does not seem possible. It would appear that if this greasy, slimy newborn infant, who looks as if he had been rescued from a sewer pit, were not immediately cleaned up, he would smell like a dead fish in twenty-four hours. What a contrast to behold him a few hours later looking so fresh and clean."

Sanford agrees that the skin is a better color and smoother if not washed or oiled. This is due to two causes. First, soap, oils, and even water are irritating to some skins; and second, freedom from handling and rubbing. What becomes of

the vernix? It almost seems to evaporate. It absorbs into the clothing. It drops off, at any rate, it disappears very rapidly. If the hair is thick and the family will be shocked by seeing vernix there, a sterile fine comb is sometimes employed.

Care must be taken that the shirt comes up into the axilla for moisture and skin surfaces in apposition may lead to irritation. The groins are the only other area to be watched. The excretions on the skin at birth seem to have a role in protecting this delicate organ against irritation and infection. Furthermore, when babies are not bathed, the common bathing and diapering table can be eliminated.

Another point in favor of the dry technique is the nursing time saved. A study of this at the Multnomah County Hospital showed a saving of five minutes on the initial care and three minutes for the subsequent daily care of each infant. This saving in a nursery with an average population of thirty amounts to an hour and a half each day, and three to four weeks of nursing time during the year.

Mouth Infections.—Thrush may be acquired during birth. The same monilium has been found in the mother's vagina in many instances. It can live, as Faber has shown, in dust collections in the nursery.

It should not spread in the modern nursery from the sporadic case, as no dust collections will be permitted and nothing that is not surgically aseptic will touch the baby's mouth.

An epidemic of an apparently new mouth infection has been reported from Baltimore. So little is known about it that I shall only mention it. The commoner mouth infections will be taken care of, I am sure, by a better aseptic technique which Dr. Christie will discuss.

Conclusion.—The large nurseries commonly found in our hospitals with bassinets touching one another, and through whose narrow passages nurses and doctors and hospital employees travel back and forth all day long, is an ideal place for the spread of infection. I doubt whether any aseptic technique can be developed which can be effective in such quarters. Small units of four to eight cribs, far enough apart to make it possible to care for a child in one without contaminating those on either side will help. A technique which will insure surgical asepsis of anything touching the baby's nose and mouth will help. The dry technique is a real help. None of these will control air-borne infections. Should the menace of an infectious enteritis continue or perhaps extend, the suggestion made by Dr. Mandel Spivek in a paper to be read before the Pediatric Section in San Francisco, of giving up the nursery entirely and putting the baby in the mother's room, may prove to be the easiest and best solution.

DR. CHRISTIE.—Dr. Durand has already indicated the reasons for calling this round table. It is unnecessary to stress further the multiple problems involved in such a discussion, but I think I can best serve my purpose here by immediately arriving at some rather definite affirmative and negative conclusions which I hope will bring out a deluge of really critical and pertinent discussion.

I am not one who would return to the days of the horse and buggy or the coal oil lamp, and I would admit that renewing the discussion of home versus hospital delivery will serve no purpose. Still I wish to point out again the distinctly abnormal conditions under which we herd together from ten to thirty newborn infants in crowded quarters which will shock the housing experts of the future. All our problems in nursery technique seem to be due to this crowding, and the solution of them inevitably entails an analysis of cost and practicability of the remedy.

The development of nursery technique is like choosing a serologic test for syphilis. It must be sufficiently sensitive to exclude all possibility of infection, it must be specific, and finally it must be adaptable to the hospital, to the patient, and to the doctor.

We must also be practical regarding aseptic technique. Isolation technique has not been devised as yet that is foolproof and entirely consistent. This immedi-

ately brings up the question of masks. In the nursery these are worn, obviously not to protect ourselves, as in isolation technique, but as a protection to the infant. If the nurses working in a nursery are to wear masks, then the mother should also wear a mask when nursing the baby. Furthermore, I am reliably informed by nursery supervisors that the wearing of a gauze mask over the nose for even a few hours will bring undesirable symptoms such as headache and nausea which soon initiate a desire on the part of the nurse to return to private duty on a surgical ward. Finally, the wearing of a mask over the nose during an entire summer day in Baltimore is a very different matter than the same procedure in cooler San Francisco. It has been shown by McKhann that the usual gauze mask is not adequate to prevent cross-infection. I do not know the answer to this question but I would like to suggest here that the new types of masks, such as the plastic or deflecting mask which is impervious to air, prevents direct infection, and allows ventilation for the wearer, may be the solution of our problem as this type of mask approaches a 75 per cent effectiveness.

Recent observations on the sterilization of air by ultraviolet light by Wells and Hart, applied by McKhann to a children's ward, revealed the inadequacy of this method for the complete sterilization of air in a ward or room. Ultraviolet light will sterilize air, but all that can be hoped for at present is a dilution of contaminated air with the ultraviolet sterilized air.

At the University of California Hospital, where the nurseries are under the supervision of the Pediatric Department, many of our past difficulties have been traced to the private service where, for one reason or another (often because of special privilege), the aseptic technique has not been as stringent as for the clinic service. We have partially, and I hope permanently, remedied this situation by breaking the active nursery group into four separate units, each infant in each unit being on individual techniques. The units are: the premature unit separated by double doors from the rest of the nursery, a clinic nursery, a private nursery, and an isolation unit for babies whose mothers have rashes, sepsis, colds, pneumonia, syphilis, gonorrhea, or are suspected of harboring other communicable diseases. If the baby should develop any abnormality needing special observation or treatment he is likewise removed to the isolation unit, where he is cared for by nurses who never enter the other nursery units. Likewise, nurses assigned to any nursery unit are never allowed to care for infants in other units.

All cleaning is done while the infants are at the breast. No visitors are ever allowed in the nursery, and the babies are shown only through glass partitions at very limited hours to a limited group. This showing of infants to visitors as well as to the mothers, is further limited during the height of the season of respiratory infections.

The supervising nurse is held strictly responsible for all aseptic technique. No one may enter the nursery in street clothes but must wear sterile mask, cap, and gown at all times. Hands must be scrubbed with soap and water before touching an infant or any of the nursery supplies. All linen, blankets, diapers, and smocks used in the nursery are sterilized. All solutions, oils, and ointments are sterilized, and only sterile garments are put on the babies.

The nursing personnel should be adequately trained and instructed to recognize and record any suspected abnormality of the infant. Various methods may be advocated for this, and I have taken the opportunity of this meeting to collect several forms from leading medical centers throughout the eastern and middle western United States. They are not presented for critical comparison but rather as an interesting exhibit of how the same information can be efficiently recorded in many different ways.

It may be noted that in one form or another there should be room for recording all instances of injury at birth, congenital abnormalities, cyanosis, fever, convulsions, pallor, jaundice, rashes, weight gains out of proportion to normal (edema),

snuffles, hemorrhage, etc., and the supervising nurse should see that any such instances are reported to the attending pediatrician. Adequate room should be available in the nursing notes for all abnormalities in the gastrointestinal system, such as failure to nurse, to take breast, or artificial feeding, character of stools, etc.

The care of the skin and mouth infections has been adequately covered by Dr. Durand. To go further giving details of my own experience would be like the doctor who reported a certain type of treatment which prevented hemorrhagic disease in 200 consecutive newborn infants. The point I am trying to make is that we lack definite scientific information to evaluate properly some of the methods we use in the care of the newborn infant. As for the evaluation of the pertussis vaccine, we need more fundamental understanding of the underlying immunology of newborn patients. If oiling the infant's skin raises the skin temperature, then we are increasing the possibility of infection by promoting a better culture medium.

In this regard I wish to add a word about nursery policy determined by weight and physical condition at birth. Dr. Durand tells me that in only about 50 per cent of hospitals he has visited do they have any means of placing the infant in a specially heated crib following delivery. I wish to make a point regarding this as I feel that every hospital should have a Nobel box or heated crib to receive infants who have just been delivered.

The greatest value for arbitrary standards to indicate prematurity is that below certain levels of weight these infants need special medical as well as nursing care. This arbitrary level for prematurity is 2500 gm., and without going into a discussion of premature care I would like to indicate the extreme importance to the infant of not allowing the body temperature to fall after delivery. In a preliminary analysis of premature mortality in those infants born at home and taken to the hospital, I have observed that the gross mortality was approximately doubled when the admission temperature was below 37° F. By use of heated premature ambulances (plus other means) Hess in Chicago has been able to reduce the inevitable premature mortality of over 50 per cent to approximately 34 per cent. This can be compared with the expected 25 per cent mortality for premature infants born in and cared for in hospital nurseries.

And so it would appear that the first duty of the delivery room nursing staff is to keep the infants warm, for some of the factors which add to premature mortality must also operate in other congenitally immature or possibly some full-term infants. Any attempt to remove vernix caseosa or to examine or measure the infants should be reserved for a time when the temperature is normal (at least 37° F.).

We do not have time nor is it within the scope of this round table on nursery technique to go into a discussion of air-conditioned nurseries. The work of Blackfan and Vaglou suggests the benefits of certain air conditions to premature infants. It has been my clinical observation and that of others that there are marked changes in the hydration of normal full-term infants when the relative humidity is very low. I believe also that we keep the temperature of our nurseries too high, which contributes to a lower humidity, subsequent dehydration, and dryness of the skin.

The nursery temperature for full-term infants should be 68° to 70° F., and the relative humidity should be between 50 and 55. I would also like to state that the production of these conditions is within the means of any institution considering a renovation or especially for those building a new nursery.

Before concluding and without meaning to appear too critical I must call your attention to the most complete and recent set of suggestions governing nursery technique which has appeared in the pediatric literature. I refer to the article of Frant and Abramson in the December, 1937, issue of the JOURNAL OF PEDIATRICS. It is entitled "Control and Prevention of Outbreaks in Hospital Nurseries." It was designed to control and prevent such disastrous epidemics as Dr. Durand has discussed and which unfortunately are spreading throughout the country with case fatality rates approaching 50 per cent.

These suggested regulations approach the ideal but do not seem always to be practical. For instance, the ratio of one nurse to two infants, as suggested by the authors quoting Brenneman, both day and night is undoubtedly a very good idea, but in dollars and cents there are few hospitals which are able financially to assume responsibility for meeting this suggestion. This recommendation is further complicated by a statement that "no nurse who dresses, bathes, or diapers the babies should feed any newborn baby." Let us take a moment to analyze these suggestions. They must mean literally that in a small private hospital where twelve infants are cared for, there would be three nurses bathing and diapering and three nurses for feeding. For three eight-hour shifts this would entail the employment of eighteen nurses to supply adequate care for the newborn infants during the twenty-four-hour period.

The routine daily inspection of nursing personnel by a regularly assigned physician and the monthly stool culture likewise seem impractical for most private and teaching hospitals. From the standpoint of hospital administration it is out of the question, and our efforts can be better directed to developing a more efficient aseptic technique for which the supervising nurse should be held strictly accountable.

Under a discussion of nursery personnel the authors suggest that "the nursing staff should be a constant one and not ever changing." In a hospital where nurses are in training, this suggestion is obviously most difficult to attain.

Now in conclusion I would like to make a plea for improvement in maternal education. This inevitably devolves upon the nursing personnel. Every mother should have not one but several demonstrations of modern methods of feeding, clothing, airing, and bathing her baby. She is an unusual patient in that she is intimately under the care of her physician for approximately a year, if we include her prenatal and post-partum care. It is possible by collaborative effort with our existing knowledge, hospital, and clinic facilities, to do a much more complete and better job in this regard, giving the mother a lasting impression of the advantages of modern obstetrics and pediatrics for herself and for her baby. The advantages of such a program in timesaving and services rendered are obvious.

DISCUSSION

DR. CHRISTIE.—I observed an epidemic of diarrhea at Johns Hopkins Hospital which began very much like a thrush. The children lost much weight, were greatly dehydrated, and had an explosive type of diarrhea. Venoclysis seemed to help more than anything else, but the mortality was 50 per cent.

CHAIRMAN DURAND.—Every delivery room should have a heated crib ready before every birth.

DR. H. K. FABER (SAN FRANCISCO).—We had a series of skin infections which lasted a period of months. We looked everywhere for the source of infection and found that it was a common bathing table. We prepared separate units and had the nurse scrub her hands and change her gown before bathing each baby. With this technique we got rid of the skin infection. We use glass caps for all nursing bottles and keep the babies separated.

DR. R. G. FLOOD (SAN FRANCISCO).—In our old hospital we were crowded but had very few skin infections. When we moved into our new hospital we began to get an increase in the number of skin infections, and had periodic outbreaks of impetigo. We looked everywhere for the source of infection and took swabs from the nurses' hands after they had scrubbed. The first swab would be negative, the second still negative, and the third swab from the same place would show staphylococcus. We decided that the soap formed a filament which covered the skin and when the filament was rubbed off, the skin still carried micro-organisms. We tried having the nurses wash their hands with Lugol's solution, and this dry technique appeals to me.

CHAIRMAN DURAND.—Tell us how you use Lugol's.

DR. FLOOD.—We have the nurse keep her hands in 3 per cent Lugol's solution until the hands are colored, and then decolorize with hyposulfite.

DR. R. P. SEITZ (SAN FRANCISCO).—I believe that many of these infections originate in the mother's room.

DR. CHRISTIE.—That is the weak point in the whole thing. We autoclave everything around the nursery and then take the baby to the mother's room where nothing is autoclaved.

DR. SEITZ.—Do not carriers serve as a menace?

DR. FLOOD.—We have abandoned carriers. The nurse has a gown for each crib and puts it on to take the baby to the mother. We tried gloves, but when gloves are wet they slip, and the nurses let a few babies fall so we quit gloves.

DR. FABER.—If nipples are not covered they become contaminated.

CHAIRMAN DURAND.—We had the nipples autoclaved, milk and all, but the babies developed a diarrhea and we quit the autoclaving.

DR. CHRISTIE.—We had an epidemic of diarrhea in the University Hospital which we thought was due to irradiated milk.

CHAIRMAN DURAND.—At the hospital in Portland no babies are bathed until they are fourteen days old. The blood is wiped off, and they sometimes use oil on genitals of girl babies.

DR. E. P. COOK (SAN JOSE, CALIF.).—Is it not true that the baby's skin is much tougher at two weeks of age?

DR. CHRISTIE.—There is no question in my mind but what that is true. I believe that oil irritates the skin. We use one-half strength tincture of green soap.

DR. G. B. KRYDER (GLENDALE, CALIF.).—How long do you leave the baby in the heated crib?

CHAIRMAN DURAND.—That depends on conditions. If there is any repair work for the mother (or trouble with the baby), the baby may be there for some time.

DR. J. M. RECTOR (SAN FRANCISCO).—Why show the baby to the mother?

DR. CHRISTIE.—When a baby's temperature goes up to normal and it begins breathing all right, it usually stays all right.

DR. R. L. PORTER (SAN FRANCISCO).—What about the obstetrician as the source of infection? I heard of one who left one hospital where he got impetigo. He went to another hospital and it happened again, and then he went to a third hospital and the impetigo still followed him. It developed that he had a streptococcic sinusitis and was probably infecting his own babies.

DR. P. J. HOWARD (DETROIT).—At the Ford Hospital, when the dry technique came out, some of our men tried it, but others refused; so we had two classes, one dry and the other, the old regime. The skin infections of the babies handled with the dry technique ran about 5 per cent, and of the babies handled with the old regime about 10 per cent. In the Women's Hospital in Detroit I have observed that their methods are about the same as ours, but their results were better.

DR. SEITZ.—At the County Hospital in San Francisco they have less skin infection than any other hospital in the city. I think this is because they have the same set of nurses year in and year out.

DR. RENA CRAWFORD (NEW ORLEANS).—At the county hospital in New Orleans they have practically no cases, but they have lots of them in the private hospitals.

DR. PORTER.—I dropped in to listen to the dermatologists yesterday afternoon and someone was telling them that negro sweat was antiseptic and, therefore,

negroes did not get fungous infections that white folks do. I wonder if the negro babies have as much impetigo as the white babies?

DR. FLOOD.—Watch a nurse who is wearing a mask. She is constantly pulling at it and changing its position. You cannot wear them all day in comfort.

DR. CHRISTIE.—I have here a transparent mask which is much easier to wear. It is called the Penn mask and is made in Germany.

DR. FLOOD.—I would like to hear a discussion on incubators.

DR. CHRISTIE.—I believe that in ten years we will have air-conditioned nurseries. They are much nearer ideal than any incubator now in use.

CHAIRMAN DURAND.—Air conditioning is a thing which we should consider.

DR. FABER.—Can anyone here tell us anything about the new incubator of Dr. Chappell of Philadelphia?

DR. CHRISTIE.—This incubator controls humidity. The nurse puts her arm into the incubator through a sleeve when she wishes to care for the baby or do anything for it.

DR. SEITZ.—This incubator almost requires an engineer to run it. You could spend the same amount of money and air condition the room and take care of several babies.

DR. HOWARD.—We made a glass box, equipped it with an electric pad, and we have a tank of oxygen and a tank of carbon dioxide and oxygen connected. We have one side open so we can get to the baby easily.

DR. L. E. RECTOR (BOSTON).—At the Boston Children's Hospital a combination respirator and incubator heated with bulbs works beautifully.

CHAIRMAN CHRISTIE.—There have been recent reports in the literature throughout the country in the past few years on diarrhea in the newborn infant. I think it well to discuss this quite fully.

DR. M. L. BLATT (CHICAGO).—The diarrheas in the newborn infant which have occurred under my observation have been cases of sepsis; they do not begin with diarrhea. Many of the patients died of bronchopneumonia. We were unable to isolate any definite organisms, and in many instances more than one organism was found in similar cases throughout the nursery. A source of infection may be from the milk supply, from the nursery, and, I think, it may probably be air borne.

DR. DURAND.—Looking for sepsis is probably right. It is interesting that not many cases occur at one time; there will be three or four cases and then a lull, to be followed by three or four cases later on. In some instances we found on examination of the stool fat droplets which were first thought to be Monilia. In these epidemic diarrheas the stools are acid, fermented, yellow, watery consistency, and practically no blood. It is the same picture seen the country over. At autopsy there is no ulceration found in the intestinal tract but marked hyperemia with terminal bronchopneumonia. Definite pathogens are not known; it may be virus.

DR. V. CULLOTA (BALTIMORE).—Are cases ever seen in older children?

DR. DURAND.—None.

DR. BLATT.—We have had patients return to the hospital twenty-one days after being discharged. These cases, like the ones occurring in the hospital, did not begin with diarrhea. There was a gradual onset, first of anorexia, fever, progressing gradually to diarrhea, etc.

CHAIRMAN CHRISTIE.—Have any breast-fed babies developed the disease?

DR. BLATT.—Some few. The feedings of breast milk, which introduce into the gastrointestinal tract *Bacillus bifidus*, seem to be of help.

DR. A. F. ABT (CHICAGO).—I am not quite so certain concerning the portal of entry in these cases. In the Michael Reese hospital in Chicago, in 1931, cases oc-

curred until the culture from the nose and throat of two nurses revealed *B. mucosus capsulatus*. The same organism was recovered from the stool. The nurses were removed, and the epidemic stopped. Tonsillectomy and adenoidectomy were performed on the nurses; they returned to the nursery, and no further cases developed. It appears from this that the portal of entry may be from the air and not through the gastrointestinal tract. I have noticed too that in the beginning the infections of these babies did not act primarily as gastrointestinal infections; more, they resemble sepsis.

DR. DURAND.—There has been some question as to whether this is a new form of disease. I think it certainly must be; it has never been seen before in epidemic form and it has occurred in forty-odd places throughout the country in the past few years. All the cases seem to be the same. There is approximately a 50 per cent mortality, so that it must be a new disease. It resembles influenza in many instances.

We might discuss somewhat the question of nursery technique and personnel. It seems that unless something is done along developing a definite technique we will be forced to give up the nurseries.

CHAIRMAN CHRISTIE.—The temperature of the nursery is usually kept at 68° to 70° F., the humidity 50 to 55 per cent. Under conditions of this sort very little clothing is put on the babies. A baby wears a shirt and diaper. If the buttocks become excoriated, the diaper is removed, and the buttocks are exposed to the sun and air. Babies never seem to be chilled or affected by this routine. The temperatures, when taken, are always normal. In the care of the skin, ammoniated mercury inunctions produce a high amount of skin irritation, but very little impetigo occurs. The dry technique is quite satisfactory. It is surprising that no irritation of the skin results as well as that the babies are devoid of odor. At the University Hospital half strength tincture of green soap bath is used.

DR. J. B. BILDERBACK (PORTLAND, ORE.).—The nurse with a cold should be removed from the nursery.

CHAIRMAN CHRISTIE.—The nurses' supervisor is invaluable and is of great help. There should be a medical examination of the nurses daily, and a monthly throat and stool culture should be made.

DR. E. G. SCHWARTZ (FORT WORTH, TEXAS).—It seems to me the question of impetigo is a climatic one. We see a number of cases in Texas in the summer only. I might say that we have had no cases of diarrhea that have been discussed. I have seen an occasional baby with sporadic bleeding from the bowel but they all seem to act well, and many times the cause for this condition is not explained.

DR. W. A. REILEY (SAN FRANCISCO).—I have seen, during the winter in San Francisco, diarrheas occurring in older children. The stools are quite loose, some mucus and occasional blood, and they are negative to organisms. Do you think these cases are the same as those occurring in the newborn infant?

DR. DURAND.—A few epidemics of diarrhea have occurred in Portland but they are not similar to those that are seen in the newborn infants, and I do not believe these cases are of a similar nature. We are very seldom troubled with diarrhea in older children; because of the cool nights we have very little effect from the hot weather or changes in the milk from heat.

DR. CULLOTA.—I have noticed very definitely that evaporated milk is more laxative now than before the milk was irradiated. Do you suppose radiation accounts for this?

DR. SAMUEL HURWITZ (SAN FRANCISCO).—Is there any particular physiologic reason for not giving cold milk to a baby; which milk has a low bacterial count?

DR. DURAND.—It does not seem right to give cold milk to a young baby, and certainly heating the milk just before it is given should not affect the count.

DR. REILEY.—Do you remove nurses who show streptococci on culture?

DR. BLATT.—They are removed from the premature room, the milk laboratory, and the newborn nursery. As nothing used in the nose and throat will be of any advantage, it is necessary that the nurses be removed.

DR. HURWITZ.—We have followed a plan in Oakland which seems to offer some help in that the mothers are delivered at the hospital and discharged on the fourth day. These periods of short hospitalization seem to give a lessened amount of trouble with babies in the nursery. I should like to ask at what time infections occur and what time do skin infections develop as a rule in the newborn infant?

DR. DURAND.—They usually occur early, about the fourth day. They are acquired by passage through the birth canal.

DR. BLATT.—Making a smaller unit and more of them will remove a large incidence of infection.

CHAIRMAN CHRISTIE.—Has anyone any suggestion to make as to how to preserve technique during circumcision rituals?

DR. DURAND.—The separation of the patient and operator by glass partitions might help to solve the problem.

DR. BLATT.—Why is humidity of the nursery necessary?

CHAIRMAN CHRISTIE.—According to the report of Dr. Blackfan and clinical evidence, it is indicated.

DR. BLATT.—We have no humidification in the premature room. The humidity is 10 to 45 per cent, and no difference has been seen.

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Secretaries.

EIGHTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

DEL MONTE, CALIF., JUNE 10 AND 11, 1938

Round Table Discussion of Diabetes Mellitus

Chairman: Dr. H. Clare Shepardson, San Francisco, Calif.
Assistant: Dr. Howard F. West, Los Angeles, Calif.

CHAIRMAN SHEPARDSON.—In bringing before this group a subject which permits of such latitude in discussion as does that of diabetes mellitus, I realize that we may stray far afield. In the past two or three years, largely as a result of the impetus provided by the discovery of protamine insulin by Hagedorn, many investigations concerning this disease have been accelerated. Yet we find from practical experience that many doctors, including pediatricians, still do not fully appreciate the incidence and symptomatology, the diagnosis nor the prognosis of the juvenile diabetic. This largely results from the fact that emphasis in discussions and in the literature has been placed on problems of management, types of diet, and of more recent months, the several types of insulin, to the more or less exclusion of these various fundamentals. Even yet we see children who have been neglected during the first weeks of symptoms, and we see mothers who have been given inadequate or misleading information about their prognosis or proper management. Tragic

examples could readily be cited, but for this representative group they would be superfluous. Nevertheless, it is felt that proper education of the physicians throughout the country is the only means of obviating this distressing state of affairs.

In order to properly open this discussion I have asked Dr. West to present to you a brief analysis of the information resulting from the study recently made by him of some 300 juvenile diabetics. Possibly these problems can be amplified later by a frank consideration of the mortality rates, the changed status of girls relative to menstrual development, and pregnancy, and the manner in which these youngsters, if adequately controlled, are able to meet the physical, economic, and sociologic complications to which they will later be subject. One problem of tremendous importance is the ability of the girl diabetic to subsequently overcome the difficulties of pregnancy, which may later ensue. This of course immediately suggests many other phases which are the result of the advent of long acting insulins. It seems obvious that the greatest accomplishment of protamine insulin has been the elimination of acidosis in childhood. Formerly it was not at all uncommon to see repeated attacks of coma in the child diabetic. These apparently will be almost entirely eliminated in the future. As a result of this improvement in the therapeutics of diabetes tremendous significance is added to the statement made by Joslin, several years ago, that "no longer is the child diabetic a dying child, but rather a living one."

Consequently we are now confronted with the fact that only rarely do children die of diabetes. It is to be expected, therefore, that the life expectancy of the child diabetic will increase immensely as a result of the use of these insulins with prolonged hypoglycemic effect.

There are other very interesting subjects concerning diabetes which, of late, have assumed considerable prominence. One of these particularly applicable to pediatricians is the association of diabetes with disturbances in function of various members of the endocrine system. Because of the increase in life expectancy of the child diabetic, and the consequent increase in the number of patients so afflicted, it seems obvious that the incidence of endocrine diseases in the juvenile diabetic population will be proportionately greater as time goes on. As you well know, there recently has been a great deal of investigative work done in several laboratories throughout the world on the relationship of various ductless glands, particularly the adenohypophysis and the adrenal cortex, to diabetes mellitus. From the relevant data available at the moment, it seems quite probable that alterations in function of either the anterior pituitary gland, or the suprarenal cortex, will profoundly effect carbohydrate metabolism. We are all aware of the effect of a hyperfunctioning thyroid on the general metabolism; consequently it is not surprising that the metabolism of carbohydrates is adversely affected in the presence of thyrotoxicosis. On the other hand, I cannot subscribe to the theory that disturbances in function of the pituitary or of the adrenal cortex, or of the thyroid gland, are causative factors in the development of diabetes. The incidence of a condition to all intents and purposes identical with diabetes mellitus is relatively high among the acromegalic population. The same statement can be made of that group of women inflicted with the suprarenogenital syndrome. It is felt that in all probability the abnormal effects evident from a hyperfunctioning acidophilic adenoma and the pituitary exercise their effect through the adrenal cortex. In order to produce diabetes under such conditions we must, for the present, hypothecate a functional disturbance of islet cell activity as a pre-existing factor in those patients afflicted with such diseases as acromegaly or the suprarenogenital syndrome and who subsequently develop an associated diabetes.

Of equal interest is the study of the reduced activity of the pituitary and the thyroid in the child diabetic. Priscilla White recently has been extremely interested in the incidence of dwarfism among her group of diabetic children. She has

used growth hormone with very gratifying results in these youngsters. Unfortunately the determination of the cause of the dwarfism among diabetic children is sometimes extremely difficult to make. The diabetes itself when improperly treated can be responsible. Bone age studies should be made in each instance, and the results thus obtained should not be ignored. Dr. White is placed in the position of having to defend her results, which, in certain instances, are open to question because she has administered, simultaneously with growth hormone, thyroid substance. And in that group of children whose dwarfism results from thyroid deficiency, it seems unnecessary to employ growth hormone to enhance their growth, for we are all familiar with the extremely favorable effects resulting from the administration of thyroid substance alone. One other factor is of serious importance; these children have all been placed on protamine zinc insulin. As a consequence, their nutrition has undoubtedly improved. This alone may account in part, at least, for some of Dr. White's results.

As a concluding feeature of this very interesting round table discussion I should like to introduce the subject of long acting insulins, with their effect not only on the disease itself, but particularly on the patient's prognosis. There seems to be no question that Hagedorn's introduction of protamine insulin has greatly enhanced the comfort of the child diabetic. Diabetes in childhood is almost uniformly a severe disease. Prior to 1935 it was necessary to give these children multiple doses of insulin during twenty-four hours in order to even partially control the disease. As a matter of fact, it was not until protamine insulin came into use that we actually realized how inadequately treated and how poorly controlled, even under the most favorable conditions, had been the child diabetic in the past. Following the institution of protamine zinc insulin the number of daily injections was reduced 50 to 75 per cent, and the control of the diabetes greatly improved. As a result, the psychic status of the child diabetic under the present regime is far superior to that which existed three or four years ago. More recently Sahyun, of Detroit, has introduced a new crystalline insulin. This substance in the hands of many investigators has proved equally satisfactory and in some respects more so than have other so-called long acting insulins.

The advantage of the newer insulins with a prolonged hypoglycemic effect have been thoroughly established. They effect a more constant, hence, better physiologic control of diabetes, a reduction in the number of daily injections of insulin, and, incidentally, frequently a considerable reduction in the total daily insulin requirement. The various disadvantages accompanying the use of these substances have been emphasized by many investigators. Suffice it to say, however, that the magnitude of those disadvantages has steadily decreased with increasing knowledge and experience in the use of these preparations. Protamine zinc insulin has produced uniformly favorable results in the treatment of diabetes. Yet, it is by no means an ideal substance. The ideal insulin should promise a lowering of blood sugar throughout the digestive period. It should be so controllable that when adequate doses are given, a maximum sugar-lowering effect would be obtained without producing hypoglycemia and the accompanying reactions or shock. For the present there seems to be some disagreement as to whether the hypoglycemic effect of crystalline insulin is sufficiently different from that of unmodified insulin to warrant its inclusion in the therapeutic armamentarium of the diabetic specialist.

Juvenile Diabetes

DR. WEST.—Fifteen years after the introduction of so radical an improvement in therapy as insulin gave to the management of juvenile diabetes would seem to be an opportune time for a review of progress. This would seem to be indicated not only for the sake of gaining what satisfaction we may, but also because experience shows that many doctors do not as yet appreciate the changed status of the diabetic

child. The extremely bad prognosis, an average expectation of life of about two years from onset of symptoms, of a decade and a half ago apparently remains fixed in many minds. This point of view is a decided handicap to the child, often delaying the institution of adequate treatment, and is especially disheartening to the anxious parents.

As an introduction to this discussion I would like to refer to the experience of my associates and myself with 328 juvenile diabetics (onset of symptoms before the age of 16 years) seen since 1917. We have included in this group children seen in private practice and in three charity hospitals and clinics. They have not all been continuously under our personal care. The results, good and bad, would, therefore, more nearly represent a cross section of community experience than individual attainment.

From the information obtained in a review of this group the following pertinent points are presented briefly:

Age of Onset.—While juvenile diabetes may become manifest at any age after birth, our patients conformed to the general experience that symptoms most frequently develop in the prepubescent years, 9 to 12 years among girls and 11 to 12 years for the boys. Onset during the first year is relatively rare (only three instances in this series). The youngest was only 8 weeks of age. No instance of congenital diabetes was seen. There is a sharp falling off in frequency during the fifteenth year.

Sex.—Also conforming to other experiences the sexes were almost equally divided with a slight preponderance of females, 174 girls and 154 boys.

Race.—Only 10.3 per cent of these children were of the Jewish race. This incidence is practically the same as found in all other series reported and is in sharp contrast to the high incidence among adult Jews. Among the non-Jews, the group included seven Mexicans, five colored persons, one Italian, one Assyrian, and one Portuguese.

Heredity.—Of all the known predisposing causes, heredity is preeminent. This information is available in 313 records, with a family history of diabetes recorded as positive in 32.8 per cent. For those with diabetes of a duration of ten or more years the family history has had time to reach 41.4 per cent. For the Jewish group it is 45.4 per cent.

Twins.—In a family under observation there is one pair of twins, each having diabetes. They are Jewish females, one having developed symptoms at 3 years and 2 months of age, the other at 3 years and 11 months. Both are living, six years and seven months and five years and ten months, respectively, since onset. Three other pairs of twins have been seen, but in only one of each pair has diabetes so far become evident. The others are under close observation.

Previous Illnesses.—H. J. John has been impressed with the importance of infections as predisposing factors in the diabetes of childhood. While acute illness and especially infections do lower carbohydrate tolerance and make existing diabetes more severe, in only about 24 per cent of the entire group did we obtain a history of an acute illness sufficiently close in time to the onset of recognizable symptoms to be considered as a possible factor in etiology or a precipitating event. As a group the records of preceding illness were little different from those obtainable from other children of similar ages. On the other hand, it must be remembered that acute symptoms of diabetes not infrequently follow immediately after one of the exanthemas or an acute respiratory infection, and even after tonsillectomy (four instances), other operations, or vaccination. In our group acute upper respiratory infections were the most common among what might be classed as precipitating events. The record shows thirty-four instances.

Presenting Symptoms and Diagnosis.—The symptoms of diabetes in the child tend to follow the classical pattern. From 316 records in which the original symp-

toms were adequately recorded we find that polyuria occurred in 91.4 per cent, polydipsia in 88.8 per cent, loss of weight and strength in 79.6 per cent, and polyphagia in 73.9 per cent. Nervous irritability and difficulty in school were not uncommon. The onset of symptoms was definitely acute in 83 per cent.

Yet, in spite of the typical nature of the symptoms and the acuteness of onset, diagnosis was much too often delayed. In 252 records sufficient data were recorded to permit the calculation of the number of days elapsing between the onset of symptoms and the discovery of glycosuria. The average delay was 55.3 days. In this the younger children fared better than those of the older age groups. The average time elapsing between onset of symptoms and diagnosis for those less than 5 years of age was 38.4 days, between 6 and 10 years, 49.2 days, while in the group more than 10 years of age symptoms had been present for an average of 77.1 days, over two and one-half months. The bathroom habits and general condition of younger children are obviously more closely observed than their older brothers and sisters. The failure to recognize the symptoms of diabetes reflects the utter astonishment of most parents when they are finally given the correct diagnosis. Doctors also are too often taken unaware and prescribe extra feedings, tonics, and vitamin concentrates or vacations before making an analysis of the urine.

The unhappy significance of this delay in diagnosis is illustrated by the fact that over 37 per cent of these children had developed a more or less severe ketosis, and an additional 21 per cent, one out of every five, were actually in coma when the diagnosis was first made. Of more particular importance is the revelation that 31.5 per cent of all deaths occurred within less than thirty days following the onset of symptoms. In the preinsulin period 50 per cent of the deaths occurred during the first month. It is obvious that the profession and also parents must be made more conscious of diabetes if these children are to be spared the hazards of delay.

Mortality.—Of 302 children whose present status is known, 248 are living and 54 or 17.9 per cent are dead, a regrettably high mortality. Insulin was first available to our group in November, 1922. Prior to this date twenty-five patients of our series had been diagnosed as diabetic. Of these twenty-five, fourteen died without benefit of insulin, a mortality of 56 per cent. Of these, eight died within a month of onset of symptoms, one lived for seven years, one for six years, and four from two years and one month to two years and eight months. Of the remaining eleven of the preinsulin group, two have died, each at five years and seven months from onset, and nine are still living. Of these nine, the onset of one was in 1920, of two in 1921, and of five in 1922. For those patients receiving no insulin, the mortality was 100 per cent. The outcome to date of 288 children for whom insulin has been available is known. Forty have died, a mortality of 13.8 per cent. If we subdivide the fifteen years of insulin experience into three five-year periods, the mortality experience is as shown in Table I.

TABLE I

PERIOD	PATIENTS			KNOWN DEATHS
	NEW PATIENTS	HELD OVER	TOTAL	
Jan. 1923—Jan. 1928	65	11	76	12 or 15.8%
Jan. 1928—Jan. 1933	122	64	186	17 or 9.1%
Jan. 1933—Aug. 1937	123	169	292	11 or 3.7%

For purposes of analysis computations have been made as of August 1, 1937. One death has occurred, however, since that date.

The steady improvement in the mortality rate is modified partly by the constant addition of new patients who have been exposed to the hazards of diabetes for a shorter period of time, but we also believe it reflects earlier diagnosis and more effective treatment.

Of particular interest is a group of eighty-three children with onset of diabetes prior to August 1, 1927, and for whom insulin has been available, in other words, those who have had an opportunity to live ten or more years. Twenty-one, or 25.3 per cent, have died. Only three of these deaths have occurred since 1930; two-thirds of the deaths of this group occurred during the first half of the period analyzed. For those exposed less than ten years the mortality has been 9.25 per cent.

Causes of Death.—Inquiry into the cause of death in this entire group shows that 60.1 per cent of the deaths must be attributed directly to diabetes. The highest incidence is naturally in the preinsulin group, 79 per cent, but even in the insulin period we must admit that for 55 per cent there is no other adequate cause. These figures are based on the total known causes of death, but the actual cause of death is unknown for five.

In the preinsulin period ten of the diabetic deaths were due to uncomplicated coma and one to a very severe ketosis complicated by gangrene of the nose and severe malnutrition.

In the insulin period twenty patients, or 50 per cent of the total deaths, died in coma. There was one death due to hypoglycemia during the early days of insulin and one with acute pancreatitis and ketosis. Twelve of the comas were uncomplicated, but in eight—two-thirds—of these insulin was stopped, refused, or the institution of treatment was too late, because of delay on the part of the parents, delay in diagnosis or, in some instances, because of both factors. Four charts gave indication of inadequate treatment; in one the treatment appeared to be adequate, but sudden death ensued, unexplained even at autopsy. In the other eight cases of coma there were severe complications, such as pneumonia, three cases; severe enteritis, one; lateral sinus thrombosis, one; otitis media, one; hyperpyrexia, one; gangrene of the bowel with peritonitis (possibly the result of huge doses of castor oil administered by the parents before admission), one.

What we may call nondiabetic deaths during the insulin period include pneumonia, three; myocardial failure after diphtheria (diabetes well controlled), one; lymphosarcoma, one; influenza, one; pertussis, one; cerebral embolism, one; drowning, one; lateral sinus thrombosis, one; pulmonary tuberculosis, one; head injury, one; and pneumococcic meningitis, one.

Duration of Life.—Prior to the use of insulin, as is well known, the average expectation of life for a diabetic child was but a little over two years from onset. Today no one knows with accuracy what it is or will be. A curve has been projected from data obtained by Dublin and Marks, of the Metropolitan Life Insurance Company, from the clinic of Dr. Joslin, indicating that the expectation is well over thirty years when onset occurs before 10 years of age.

Sixty-two, or 25 per cent, of our group have already lived ten years or more, the longest nearly eighteen years; while 156, or 62.5 per cent, have lived five years or more; and 87.8 per cent have passed the two-year mark. At least nine more patients would be added to the ten-year group if we were to carry our analysis to June, 1938, instead of closing it on August 1, 1937.

Nonfatal Complications.—There is perhaps no better way to evaluate both the hardihood of these modern diabetic youngsters and the efficacy of present-day treatment than to consider some of the many complications that have been successfully met during the course of their diabetes. The list is much too long for a detailed report at this time. Only some of the more severe tests are reported.

There are 71 individuals who have survived coma, 32 of them on more than one occasion. An additional 171 have experienced more or less severe ketosis. There have been 40 repeaters. Other complications met successfully were: measles, in 38 patients; mumps, 14; chicken pox, 25; pertussis, 19; pneumonia, 7; scarlet fever, 4; diphtheria, 3; tonsillitis, 46; appendicitis, 12; typhoid fever, 1; upper respiratory infections of note, 104; enteritis, 25; pulmonary tuberculosis, 1; poliomyelitis,

1; tonsillectomy, 42; appendectomy, 8; gangrene of the nose, 3; tracheotomy, 1; operation for squint, 1; extensive burns with skin grafting, 1; fracture of leg, 2; fracture of spine, 1; mastoidectomy, 1; removal of ovarian cyst, 1; herniotomy, 1; traumatic rupture of spleen with laparotomy, 1.

Retinitis has been observed in 2 patients and cataract in only one. In only 1 patient has there been detected any evidence of arteriosclerosis of clinical importance.

Of all the complications the most interesting and perhaps the most significant is pregnancy.

Prior to the insulin period girls developing diabetes before the sixteenth year did not live long enough, as a rule, to marry. Sexual development was delayed and total amenorrhea was the rule rather than the exception.

A new generation has been added to medical history. These girls are beginning to marry and to have children. In this group there have been at least thirteen pregnancies in eight individuals. There have been six cesarean sections for five mothers. One abortion was induced because of intractable ketosis and vomiting before the patient came under our observation. There has been no maternal mortality. (Two pregnancies have not reached term.)

The increasing frequency of pregnancy among diabetic women is adding new problems for the pediatrician.

The newborn infants of diabetic mothers may be oversized, fat, and flabby. Congenital anomalies are somewhat more frequent than the general average. The newborn infants of diabetic mothers are apparently somewhat more prone to develop hypoglycemia of clinical significance than other infants. However, the importance of spontaneous hypoglycemia among all newborn infants has but recently begun to be appreciated. Emergency treatment may be indicated to prevent deaths. To date we have not observed diabetes developing in the offspring of a mother diabetic at the time of delivery. One parent of each of three of the children in this series has developed diabetes since the onset in the child.

DISCUSSION

DR. A. E. FISCHER (NEW YORK CITY).—Were the twins identical?

DR. WEST.—They were; however, in many cases reported, twins were not identical

CHAIRMAN SHEPARDSON.—The factor of heredity is much higher than heretofore. Dr. West shows a present incidence of 32.8 per cent.

DR. LEE COHN (SAN FRANCISCO).—What is the attitude toward pregnancy for a woman having diabetes since childhood?

CHAIRMAN SHEPARDSON.—If there is no diabetic history in the paternal family, we advise pregnancy. If the history is positive in the paternal family, we advise against pregnancy. Diabetes is a recessive Mendelian character. If limited to one side of the family, the recessive will not become dominant. The mother could not reasonably be sterilized.

DR. WEST.—Joslin states that if the mother is prohibited from becoming pregnant, then all of her brothers and sisters should not have children.

DR. COHN.—This is a great economic problem.

CHAIRMAN SHEPARDSON.—Also it is a great social problem. The diabetic child's life is pathetic, and probably no child would want to come into life under such conditions.

DR. WEST.—If the diabetic mother has one normal child sterilization could be advised.

CHAIRMAN SHEPARDSON.—Dr. West has significantly pointed out the results of a delayed diagnosis. The adult internist sees more sick children than the pedi-

atrician; he should keep diabetes of childhood in mind in diagnosis. He is often at fault for the delay in diagnosis.

On the other hand, many parents are at fault in withholding insulin therapy.

Death in coma is due to carelessness. Sixty per cent of Dr. West's fatal cases were patients with coma, and this should never occur. Severe acidosis also is inexcusable.

DR. COHN.—The coma cases were under your care, were they not?

DR. WEST.—Not always. This one 15-year-old boy was operated for hernia by another physician who failed to care for the diabetes.

DR. P. J. HOWARD (DETROIT).—Did you note any relation between enuresis and diabetes?

DR. WEST.—We have seen a few diabetics with enuresis but without glycosuria at the time. Occasionally other enuretics have had mild glycosuria but not true diabetes.

DR. HOWARD.—Is there any contraindication to general anesthesia for surgery?

DR. WEST.—No. Surgery, if it helps elimination of infection, should be done.

CHAIRMAN SHEPARDSON.—Any necessary surgery can be done if the diabetes is under good control. Anesthesia is not a major question.

DR. COHN.—What are your criteria for good control?

CHAIRMAN SHEPARDSON.—Blood sugar determination is not absolutely essential. If there is no glycosuria the patient is burning his blood sugar efficiently.

DR. COHN.—Does diabetes occur without glycosuria?

CHAIRMAN SHEPARDSON.—Probably not in childhood. If so, it is very rare. The symptoms will help in diagnosis.

DR. HOWARD.—Is glucose tolerance essential in every diabetic suspect?

CHAIRMAN SHEPARDSON.—No. But a fasting test and one after a high carbohydrate meal could be done first. If the fasting test is high the glucose tolerance need not be done.

DR. W. A. REILLY (SAN FRANCISCO).—What is your preparation for surgery?

DR. WEST.—Emergency surgery can be done immediately. In the meantime, we give enough carbohydrate and adequate insulin to control ketosis. Urinalysis is important. A blood sugar can be done but it is not absolutely necessary. The important thing is sufficient fluid and a good storage of glucose in the liver. For elective cases, store carbohydrate ahead of time in liver and have diabetes under control.

CHAIRMAN SHEPARDSON.—Often in comatose diabetics the abdomen (rigid abdomen, 100,000 white blood count, acidosis with vomiting and pains) may simulate surgical abdomen. These patients can be treated medically from three to five hours and then operated if doubt still exists. The mortality is less if the infection can be relieved surgically.

DR. R. S. LEET (OAKLAND, CALIF.).—What do you think of the substitutes for insulin?

CHAIRMAN SHEPARDSON.—There are none. Hexylresorcinol and inulin are no good. Synthaline causes liver diseases. Myrtillin is not at all reliable. Mehlitol is a fraud.

DR. COHN.—Are pathologic changes definite in infancy?

CHAIRMAN SHEPARDSON.—Very often they are not.

DR. REILLY.—Do diabetic children later develop polyglandular syndromes?

DR. WEST.—Some adolescent girls become obese and develop amenorrhea. Thus other glands can become hypofunctional as well as the pancreas.

DR. REILLY.—Do these girls grow normally?

DR. WEST.—A few fail to grow well. This is probably a question of undernutrition, even though they are obese. Since diabetic children have been fed more liberally, the dwarfism has disappeared. Adequate growth and weight (short of obesity) is the desideratum. The skeletal dwarfism was fundamentally a nutritional deficiency.

DR. J. W. BRUCE (LOUISVILLE, KY.).—What do you think of free choice of diet and control with protamine insulinate?

CHAIRMAN SHEPARDSON.—All diets should include adequate calories for occupation or growth. Secondly, there must be an adequate amount of protein. Before insulin was introduced sugar and carbohydrate were taken out of the diet; the diet was mainly high in protein and fat. In 1914 Frederick Allen postulated that total calories should be lessened. In 1922, when insulin was first in use, carbohydrate was put into the diet to the extent of about 50 gm. daily.

There are three schemes of diet. Newburgh raised the fat to 100 gm. daily. He and Gellan, in New York, suggested a high fat diet because they thought blood sugar would be more stable, and complications like arteriosclerosis would be less frequent. Rabinowitch, Allen, Bast, Joslin, etc., all have used variable diets, and their patients do quite well. I have stuck to an intermediate course and use about 150 gm. of carbohydrate. One can use whatever satisfies the patients and keeps them happy. Of course the blood sugar and urine have to stay within normal limits. Any diet which does not violate the ketogenic-antiketogenic ratio is satisfactory if palatable. It probably matters little if a high fat, low carbohydrate diet or the reverse is used. Much depends on the patient and the physician.

DR. WEST.—What is a diabetic diet? It is only a quantitative diet, which free choice of diet is not. Insulin dosage always has to be anticipated. This cannot be done with the free choice diet if the insulin is used before meals, as it usually has to be. If the patient would take the same amount of protein, carbohydrate, and fat on a free choice diet every day, then the insulin dosage could be satisfactorily anticipated.

CHAIRMAN SHEPARDSON.—All diabetic diets are weighed diets. There is normally a 10 per cent variation with weighing. Too many variables already exist in diabetic therapy without using the free choice diet. Blood sugar will vary greatly. The hypoglycemia is far more dangerous than hyperglycemia.

We will learn much from the use of insulin for dementia precox.

DR. BRUCE.—Is protamine insulin better than insulin for children?

CHAIRMAN SHEPARDSON.—This is hard to answer. Neither one is adequate. I would stay with regular insulin; also it acts more quickly. I have to use the same number of injections with protamine as with old insulin. Few children can get along with a single injection; if so, old insulin is still adequate.

DR. BRUCE.—How do you counteract protamine reactions in early morning?

CHAIRMAN SHEPARDSON.—I would try diet as ⅕, ⅖, and ⅖ at night. At 6:00 P.M. give 60 per cent of the ⅖ and 40 per cent at 10:00 P.M. Extra crackers can be given at early morning if reactions occur. Give less of protamine before breakfast and give some regular insulin after breakfast for short immediate use. Crystalline insulin is very good and possibly superior to protamine insulin in that less injections are required.

DR. BRUCE.—How much exercise do you recommend?

CHAIRMAN SHEPARDSON.—It depends on the child. Some children may develop hypoglycemia in the morning if overexercised. However, exercise in general should not be restricted.

DR. P. F. DWAN (MINNEAPOLIS).—What percentage of your cases were treated with protamine insulin?

DR. WEST.—The majority have had it during the last two years. There are very few who are on one dose of protamine alone. We do not share the enthusiasm which prevailed several years ago, but we do feel that protamine has definite advantages.

DR. S. R. KALISKI (SAN ANTONIO).—Can you follow a case to your own satisfaction solely by the micromethod of sugar determination?

CHAIRMAN SHEPARDSON.—Yes.

DR. KALISKI.—At what time of day do you give protamine insulin?

CHAIRMAN SHEPARDSON.—Almost uniformly before breakfast.

DR. C. A. BOST (SAN FRANCISCO).—How do you handle new patients in the office?

CHAIRMAN SHEPARDSON.—If marked ketosis is present, they are better off in the hospital. I put them on reduced diets and small doses of regular insulin as required. If definite coma or drowsiness exists, plenty of fluid and saline solution should be used. Insulin is given in amounts depending on the glycosuria.

DR. A. A. WALKER (BIRMINGHAM, ALA.).—How much?

CHAIRMAN SHEPARDSON.—In general about 25 units for a brick red reduction, 20 for orange, 15 for yellow, 10 for green reduction. This can be varied depending on the child's weight.

DR. REILLY.—Do you recommend alkali for coma?

CHAIRMAN SHEPARDSON.—I do not use it. Those who do, use so little that it is not effective. Salt solution does well; alkali may produce anuria. Water and sodium chloride are very important and almost equal to insulin.

DR. REILLY.—How do you manage diabetic coma?

CHAIRMAN SHEPARDSON.—The patient in uncomplicated coma is a patient in shock. It is essential that this be combated immediately by warmth, administration of fluids, and the use of drugs, such as caffeine, to support the failing circulation. Insulin can be immediately started in small doses, i.e., 25 units every half hour until the glycosuria begins to diminish. The small insulin doses are then rapidly reduced. The previously mentioned doses, of course, will be reduced depending on the ratio of the child's weight to a normal adult weight.

The two important procedures following the institution of shock therapy are the administration of adequate amounts of fluid in the form of normal salt solution in the use of unmodified insulin in frequently repeated relatively small doses. It is difficult to tell which of these two is the more important. As soon as the patient is sufficiently conscious to swallow, carbohydrate fluids are given by mouth. Early in the course of treatment the stomach should be washed.

The dosage of insulin can be regulated quite safely by observing the urine. Of course a blood sugar determination is very helpful when available.

DR. REILLY.—Do you use glucose infusions during coma?

CHAIRMAN SHEPARDSON.—No. Given a patient with high blood sugar, the intravenous injection of glucose may produce anuria; also one does not know exactly how the insulin will act. If too effective the best indicator, glycosuria, is not available. The clinician should never think first of glucose administration in diabetic coma; only very rarely is it needed, and its use may produce untoward and extremely undesirable effects. Likewise alkalies are not used.

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Secretaries.

Comments

THE National Health Conference may well be the greatest event in medical science which has happened in our time." Even if this statement of Dr. Parran, Surgeon General of the United States Public Health Service, in a network broadcast during the Conference held in Washington, July 18, 19 and 20, should prove to be a marked exaggeration, nevertheless its significance to American medicine is beyond question. For the first time the medical profession met face to face with the specific demands of the public. And these demands were put forward in no pleading, hesitant way.

Although some of the discussion of the Conference was carried as news in the press, and will be featured in a number of journals, of both a medical and social nature, it is the feeling of some of the Editorial Board and officers of the Academy that a report of the Conference in THE JOURNAL OF PEDIATRICS might help for a better, unprejudiced understanding of what took place and is taking place. Three Fellows of the Academy were present as "Members of the Conference," Allan Butler, Clifford Grulee and Borden Veeder. A report written by Veeder of the Editorial Board appears as a special article on page 400 of this issue. The report attempts to present what took place, what was said and done, and to avoid any critical analysis or expression of personal viewpoint. The report is based on notes taken at the Conference and on stenographic copies of the remarks of a number who took part in the discussion. Many exact quotations have been used and care has been taken that in no instance the quotations give a false interpretation or meaning by removing them from the context.

The pediatricians have been the outstanding group in the medical profession who have recognized "medical needs," and who have whole-heartedly recognized their responsibility in the inauguration and support of measures aimed for the betterment of the health of American children, and thus in turn for the nation as a whole.

The planned extension of the work for children under the direction of the Children's Bureau has been approved by the Academy, and there is no question but that the Fellowship will continue to cooperate as they have done in the past and are now doing.